Alcohol use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence

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1 Preface

This guideline is one of three pieces of NICE guidance addressing alcohol-use disorders. The present guideline addresses the management of alcohol dependence and harmful alcohol use in people 10 years and older including: assessment, pharmacological interventions, psychological and psychosocial interventions, and settings of assisted withdrawal and rehabilitation. The two other NICE guidelines address: 1) The prevention of alcohol-use disorders in people 10 years and older, which is public health guidance on the price of alcohol, advertising and availability of alcohol, how best to detect alcohol misuse both in and outside primary care and brief interventions to manage alcohol misuse in these settings (NICE, 2010a), and 2) The assessment and clinical management in people 10 years and older of acute alcohol withdrawal, including delirium tremens, liver damage, acute and chronic pancreatitis and the management of Wernicke's encephalopathy (NICE, 2010b).

This guideline will sometimes use the term alcohol misuse, which will encompass both people with alcohol dependence and harmful alcohol use.

The guideline recommendations have been developed by a multidisciplinary team of healthcare professionals, lay member, service user and carer representatives, and guideline methodologists, after careful consideration of the best available evidence. It is intended that the guideline will be useful to clinicians and service commissioners in providing and planning high-quality care for people who misuse alcohol while also emphasising the importance of the experience of care for them and their carers.

Although the evidence base is expanding, there are also a number of gaps in the literature. The guideline makes a number of research recommendations specifically to address gaps in the evidence base. In the meantime, it is hoped that the guideline will assist clinicians, people who misuse alcohol and their carers by identifying the merits of particular treatment approaches where the evidence from research and clinical experience exists.

1.1 National guideline

1.1.1 What are clinical practice guidelines?

Clinical practice guidelines are 'systematically developed statements that assist clinicians and patients in making decisions about appropriate treatment for specific conditions' (Mann, 1996). They are derived from the best available research evidence, using predetermined and systematic methods to identify and evaluate the evidence relating to the specific condition in question. Where evidence is lacking, the guidelines incorporate statements and recommendations based upon the consensus statements developed by the Guideline Development Group (GDG).

Clinical guidelines are intended to improve the process and outcomes of healthcare in a number of different ways. They can:

- provide up-to-date evidence-based recommendations for the management of conditions and disorders by healthcare professionals

- be used as the basis to set standards to assess the practice of healthcare professionals
- form the basis for education and training of healthcare professionals
- assist people with alcohol dependence and harmful alcohol use and their carers in making informed decisions about their treatment and care
- improve communication between healthcare professionals, people with alcohol dependence and harmful alcohol use and their carers
- help identify priority areas for further research.

1.1.2 Uses and limitations of clinical guidelines

Guidelines are not a substitute for professional knowledge and clinical judgement. They can be limited in their usefulness and applicability by a number of different factors: the availability of high-quality research evidence, the quality of the methodology used in the development of the guideline, the generalisability of research findings and the uniqueness of individuals who misuse alcohol.

Although the quality of research in this field is variable, the methodology used here reflects current international understanding on the appropriate practice for guideline development (AGREE: Appraisal of Guidelines for Research and Evaluation Instrument; www.agreecollaboration.org), ensuring the collection and selection of the best research evidence available and the systematic generation of treatment recommendations applicable to the majority of people with these disorders and situations. However, there will always be some people and situations for which clinical guideline recommendations are not readily applicable. This guideline does not, therefore, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual, in consultation with the person with alcohol dependence and harmful alcohol use or their carer.

In addition to the clinical evidence, cost-effectiveness information, where available, is taken into account in the generation of statements and recommendations of the clinical guidelines. While national guidelines are concerned with clinical and cost effectiveness, issues of affordability and implementation costs are to be determined by the National Health Service (NHS).

In using guidelines, it is important to remember that the absence of empirical evidence for the effectiveness of a particular intervention is not the same as evidence for ineffectiveness. In addition, of particular relevance in mental health, evidence-based treatments are often delivered within the context of an overall treatment programme including a range of activities, the purpose of which may be to help engage the person and to provide an appropriate context for the delivery of specific interventions. It is important to maintain and enhance the service context in which these interventions are delivered; otherwise the specific benefits of effective interventions will be lost. Indeed, the importance of organising care in order to support and encourage a good therapeutic relationship is at times as important as the specific treatments offered.

1.1.3 Why develop national guidelines?

The National Institute for Health and Clinical Excellence (NICE) was established as a Special Health Authority for England and Wales in 1999, with a remit to provide a single source of authoritative and reliable guidance for patients, professionals and the public. NICE guidance aims to improve standards of care, to diminish unacceptable variations in the provision and quality of care across the NHS and to ensure that the health service is patient centred. All guidance is developed in a transparent and collaborative manner using the best available evidence and involving all relevant stakeholders.

NICE generates guidance in a number of different ways, three of which are relevant here. First, national guidance is produced by the Technology Appraisal Committee to give robust advice about a particular treatment, intervention, procedure or other health technology. Second, NICE commissions public health intervention guidance focused on types of activity (interventions) that help to reduce people's risk of developing a disease or condition or help to promote or maintain a healthy lifestyle. Third, NICE commissions the production of national clinical practice guidelines focused upon the overall treatment and management of a specific condition. To enable this latter development, NICE has established seven National Collaborating Centres in conjunction with a range of professional organisations involved in healthcare.

1.1.4 The National Collaborating Centre for Mental Health

This guideline has been commissioned by NICE and developed within the National Collaborating Centre for Mental Health (NCCMH). The NCCMH is a collaboration of the professional organisations involved in the field of mental health, national patient and carer organisations, and a number of academic institutions and NICE. The NCCMH is funded by NICE and is led by a partnership between the Royal College of Psychiatrists' Research and Training Unit and the British Psychological Society's equivalent unit (Centre for Outcomes Research and Effectiveness).

1.1.5 From national guidelines to local implementation

Once a national guideline has been published and disseminated, local healthcare groups will be expected to produce a plan and identify resources for implementation, along with appropriate timetables. Subsequently, a multidisciplinary group involving commissioners of healthcare, primary care and specialist mental health professionals, people who misuse alcohol and carers should undertake the translation of the implementation plan locally taking into account both the recommendations set out in this guideline and the priorities set in the National Service Framework for Mental Health (Department of Health, 1999b) and related documentation. The nature and pace of the local plan will reflect local healthcare needs and the nature of existing services; full implementation may take a considerable time, especially where substantial training needs are identified.

1.1.6 Auditing the implementation of guidelines

This guideline identifies key areas of clinical practice and service delivery for local and national audit. Although the generation of audit standards is an important and necessary step in the implementation of this guidance, a more broadly based implementation strategy will be developed. Nevertheless, it should be noted that the Care Quality Commission will monitor the extent to which Primary Care Trusts,

trusts responsible for mental health and social care and Health Authorities have implemented these guidelines.

1.2 The national alcohol dependence and harmful alcohol use guideline

1.2.1 Who has developed this guideline?

The GDG was convened by the NCCMH and supported by funding from NICE. The GDG included lay member, service user and carer representatives, and professionals from psychiatry, clinical psychology, general practice, nursing and psychiatric pharmacy.

Staff from the NCCMH provided leadership and support throughout the process of guideline development, undertaking systematic searches, information retrieval, appraisal and systematic review of the evidence. Members of the GDG received training in the process of guideline development from NCCMH staff, and the service user and carer representatives received training and support from the NICE Patient and Public Involvement Programme. The NICE Guidelines Technical Advisor provided advice and assistance regarding aspects of the guideline development process.

All GDG members made formal declarations of interest at the outset, which were updated at every GDG meeting. The GDG met a total of fourteen times throughout the process of guideline development. It met as a whole, but key topics were led by a national expert in the relevant topic. The GDG was supported by the NCCMH technical team, with additional expert advice from special advisors where needed. The group oversaw the production and synthesis of research evidence before presentation. All statements and recommendations in this guideline have been generated and agreed by the whole GDG.

1.2.2 For whom is this guideline intended?

This guideline is relevant for adults with alcohol dependence and harmful alcohol use as the primary diagnosis and covers the care provided by primary, community, secondary, tertiary and other healthcare professionals who have direct contact with, and make decisions concerning the care of, adults with alcohol dependence and harmful alcohol use.

The guideline will also be relevant to the work, but will not specifically cover the practice, of those in:

- occupational health services
- social services
- forensic services
- the independent sector.

The experience of alcohol misuse can affect the whole family and often the community. The guideline recognises the role of both in the treatment and support of people with alcohol dependence and harmful alcohol use.

1.2.3 Specific aims of this guideline

The guideline makes recommendations for the treatment and management of alcohol dependence and harmful alcohol use. It aims to:

- improve access and engagement with treatment and services for people who misuse alcohol
- evaluate the role of specific psychological and psychosocial interventions in the treatment of dependence and harmful alcohol use
- evaluate the role of specific pharmacological interventions in the treatment of alcohol dependence and harmful alcohol use
- integrate the above to provide best-practice advice on the care of people with alcohol dependence and harmful alcohol use and their family and carers
- promote the implementation of best clinical practice through the development of recommendations tailored to the requirements of the NHS in England and Wales.

1.2.4 The structure of this guideline

The guideline is divided into chapters, each covering a set of related topics. The first three chapters provide an introduction to guidelines, the topic and the methods used to update this guideline. Chapters 5 to 7 provide the evidence that underpins the recommendations about the treatment and management of alcohol misuse, with Chapter 4 providing personal accounts from people with alcohol problems and carers, which offer an insight into their experience.

Each evidence chapter begins with a general introduction to the topic that sets the recommendations in context. Depending on the nature of the evidence, narrative reviews or meta-analyses were conducted, and the structure of the chapters varies accordingly. Where appropriate, details about current practice, the evidence base and any research limitations are provided. Where meta-analyses were conducted, information is given about the review protocol and studies included in the review. Clinical evidence summaries are then used to summarise the data presented. Health economic evidence is then presented (where appropriate), followed by a section (from evidence to recommendations) that draws together the clinical and health economic evidence and provides a rationale for the recommendations. On the CD-ROM, further details are provided about included/excluded studies, the evidence, and the previous guideline methodology (see for Table 1 for details).

Table 1: Appendices on CD-ROM.	
Clinical study characteristics tables	Appendix 16
Clinical evidence forest plots	Appendix 17
GRADE profiles	Appendix 18
Evidence tables for economic studies	Appendix 19

2. Alcohol dependence and harmful alcohol use

2.1 Introduction

This guideline is concerned with the identification, assessment and management of alcohol dependence and harmful alcohol use[1] in people aged 10 years and older. The beverage alcohol is consumed by 87% of the UK population, nearly 40 million people (Fuller, 2008). Drinking alcohol is widely socially accepted and associated with relaxation and pleasure, and many people drink alcohol without experiencing harmful effects. However, a growing number of people experience physical, social and psychological harmful effects of alcohol. Some 26% of the adult population in England, including 38% of men and 16% of women, consumes alcohol in a way that is potentially or actually harmful to their health or well being (Drummond *et al*., 2005). Of this group, 4% of adults are alcohol dependent (6% men; 2% women) which involves a significant degree of addiction to alcohol, making it difficult for them to reduce their drinking or abstain in spite of increasingly serious harm. Alcohol dependence and harmful alcohol use are recognised as mental health disorders by the World Health Organisation (WHO, 1992). Although not an official diagnostic term, we will use 'alcohol misuse' as a collective term to encompass alcohol dependence and harmful alcohol use throughout this guideline.

The harm related to alcohol is a consequence of its toxic and dependence producing properties. Ethanol (or ethyl alcohol) in beverage alcohol is produced by the fermentation of sugar by yeast. It is a small molecule which is rapidly absorbed in the gut and is distributed to, and has effects in, every part of the body. Most organs in the body can be affected by the toxic effects of alcohol, resulting in more than 60 different diseases. The risks of developing these diseases are related to the amount of alcohol consumed over time, with different diseases having different levels of risk. For example, the risk of developing breast cancer increases in a linear way, in which even small amounts of alcohol increase risk. With alcoholic liver disease the risk is curvilinear, with harm increasing more steeply with increasing alcohol consumption. In the case of cardiovascular disease, a modest beneficial effect has been reported with moderate amounts of alcohol, although recent research suggests this effect may have been overestimated (Oforei Adjei *et al*., 2007). During pregnancy alcohol can cause harm to the foetus, which can cause prematurity, stillbirth, and the developmental disorder, Foetal Alcohol Syndrome.

Alcohol is rapidly absorbed in the gut and reaches the brain soon after drinking. This rapidly leads to changes in coordination which increase the risk of accidents and injuries, particularly when driving a vehicle or operating machinery, and when combined with other sedative drugs. Its adverse effects on mood and judgment can

[1] Several terms including 'alcoholism', 'alcohol addiction', 'alcohol abuse', and 'problem drinking' have been used in the past to describe disorders related to alcohol consumption. However, 'alcohol dependence', and 'harmful alcohol use' are used throughout this guideline to be consistent with the World Health Organisation's International Classification of Mental Disorders, 10th Revision (WHO, 1992).

increase the risk of violence and violent crime. Heavy chronic alcohol consumption increases the risk of mental health disorders including depression, anxiety, psychosis, and alcohol dependence, and increases the risk of suicide. Both acute and chronic heavy drinking can lead to a wide range of social problems including domestic violence and marital breakdown, child abuse and neglect, absenteeism and job loss (Drummond, 1990; Prime Minister's Strategy Unit, 2003).

The harm related to alcohol has been increasing in the UK in the past 3 decades. Deaths from alcoholic liver disease have doubled since 1980 (Leon & McCambridge, 2006) compared with a decrease in many other European countries. Alcohol related hospital admissions increased by 71% between 2003 and 2007, accounting for to 811,443 admissions with a primary or secondary diagnosis wholly or partly related to alcohol in 2006-07, 6% of all hospital admissions (NAO, 2008).

Alcohol is a psychoactive substance with properties known to cause dependence (or addiction). If compared within the framework of the 1971 Convention on Psychotropic Substances, alcohol would qualify as a dependence producing substance warranting international control (United Nations, 1977; Oforei-Adjei *et al*., 2007). Alcohol shares its dependence producing mechanism with other psychoactive addictive drugs. Although a smaller proportion of the population who consume alcohol become dependent than is the case with Class A drugs such as cocaine, it is nevertheless a significant problem due to much the larger number of people who consume alcohol (Kandel *et al*., 1997).

Alcohol presents particularly serious consequences in young people due to a higher level of vulnerability to the adverse effects of alcohol. Heavy drinking in adolescence can affect brain development and has a higher risk of organ damage in the developing body (Ziegler *et al*., 2005). Alcohol consumption before the age of 13, for example, is associated with a four fold increased risk of alcohol dependence in adulthood (Dawson *et al*., 2008; Hingson & Zha, 2009). Other groups who are also at higher risk of alcohol-related harm include: the elderly, those with pre-existing illnesses or who are taking a range of medicines that interact with alcohol, and the socially disadvantaged (O'Connell *et al*., 2003; Marmot *et al*., 2010).

2.2 Definitions

The definition of harmful alcohol use in this guideline is that of the World Health Organisation's International Classification of Mental Disorders, 10th Revision (ICD-10; WHO, 1992):

"a pattern of psychoactive substance use that is causing damage to health. The damage may be physical (e.g. hepatitis) or mental (e.g. depressive episodes secondary to heavy alcohol intake). Harmful use commonly, but not invariably, has adverse social consequences; social consequences in themselves, however, are not sufficient to justify a diagnosis of harmful use."

The term was introduced in ICD-I0 and replaced "non-dependent use" as a diagnostic term. The closest equivalent in other diagnostic systems (e.g. DSM-IV, American Psychiatric Association, 1994) is alcohol abuse, which usually includes social consequences.

The term "hazardous use" appeared in the draft version of ICD-10 to indicate a pattern of substance use that increases the risk of harmful consequences for the user. This is not a current diagnostic term within ICD-10. Nevertheless it continues to be used by WHO in its public health programme (WHO, 2010a; 2010b).

In ICD-10 the 'dependence syndrome' is defined as:

"a cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state."

In more common language and in earlier disease classification systems this has been referred to as 'alcoholism'. However the term 'alcohol dependence' is preferred as it is more precise and more reliably defined and measured using the criteria of ICD-10 (Box 1).

Box 1. ICD-10 Diagnostic guidelines for the Dependence Syndrome (WHO, 1992)

A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:

(a) a strong desire or sense of compulsion to take the substance;
(b) difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use;
(c) a physiological withdrawal state when substance use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
(d) evidence of tolerance, such that increased doses of the psychoactive substances are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol- and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill nontolerant users);
(e) progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
(f) persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

Narrowing of the personal repertoire of patterns of psychoactive substance use has also been described as a characteristic feature (e.g. a tendency to drink alcoholic drinks in the same way on weekdays and weekends, regardless of social constraints that determine appropriate drinking behaviour).

It is an essential characteristic of the dependence syndrome that either psychoactive substance taking or a desire to take a particular substance should be present; the subjective awareness of compulsion to use drugs is most commonly seen during attempts to stop or control substance use.

Alcohol dependence is also a category of mental disorder in DSM-IV (APA, 1994), although the criteria are slightly different from those used by ICD-10. For example a strong desire or compulsion to use substances is not included in DSM-IV, whereas more criteria relate to harmful consequences of use.

2.3 Epidemiology of alcohol

2.3.1 Prevalence

Alcohol is consumed by 87% of the UK population in the past year (Fuller, 2008). Amongst those who are current abstainers, some have never consumed alcohol for religious, cultural or other reasons, and some have consumed alcohol in the past but not in the past year. This latter group includes people who have been harmful drinkers or alcohol dependent in the past and who have stopped because of experiencing the harmful effects of alcohol.

Amongst those who currently consume alcohol there is a wide spectrum of alcohol consumption from the majority who are moderate drinkers through to a smaller number of people who regularly consume a litre of spirits per day or more, who will typically be severely alcohol dependent. However, it is important to note that most of the alcohol consumed by the population is drunk by a minority of heavy drinkers.

The Department of Health has introduced definitions that relate to different levels of drinking risk. One UK unit of alcohol is defined as 8g (or 10ml) of pure ethanol.[2] The Department of Health recommends that adult men should not regularly drink more than four units of alcohol per day, and women, three units (DH, 1995). This definition implies the need for alcohol free or lower alcohol consumption days. Below this level alcohol consumption is regarded a 'low risk' in terms of health or social harms. The Government's advice on alcohol in pregnancy is to abstain (DH, 2008). The Royal Colleges' advice is to drink less than 21 Units of alcohol per week in men and 14 units in women, which is consistent with Government advice if alcohol free days are included in the weekly drinking pattern (Royal College of Psychiatrists, 1986). Those people who drink above these levels but have not yet experienced alcohol-related harm are regarded as hazardous drinkers: i.e. their drinking is at a level which increases the risk of harm in the future. These recommendations are based on longitudinal research on the impact of different levels of alcohol consumption on mortality. Above 50 units of alcohol per day in men and 35 units in women is regarded as "definitely harmful" (RCPsych, 1986). Those drinking more than eight units per day in men and six units in women are regarded by the Government as 'binge drinkers' (Prime Minister's Strategy Unit, 2004). Again these definitions are based on longitudinal research on the effects of alcohol consumption on adverse consequences including accidents, injuries and other forms of harm.

Most of the data on the English population's drinking patterns comes from the General Household Survey, the Health Survey for England, and the Psychiatric

[2] The UK unit definition differs from definitions of standard drinks in some other countries. For example a UK unit contains 2/3 of the quantity of ethanol compared to a US 'standard drink'.

Morbidity Survey (Goddard, 2006; Craig & Mindell, 2008; McManus *et al*., 2009). In terms of hazardous drinking, in 2005 25% of adult men were drinking between 22 and 50 units per week and 15% of adult women were drinking between 15 and 35 units (Goddard, 2006). A further 6% of men and 2% of women were harmful drinkers, drinking above 50 and 35 units per week respectively (Jones *et al*., 2007). In addition 17% of adult men and 7% of women met the Government's criteria for binge drinking. There were regional variations in the prevalence of these drinking patterns. Hazardous drinking varied from 21% in London to 28% in Yorkshire and Humber, and in women from 11% in London to 18% in the North West. Harmful drinking in men varied from 5% in the East Midlands to 7% in the North East, and in women from 1% in East of England to 3% in the South East. Binge drinking varied from 13% in men and 5% in women in London to 23% in men and 12% in women in Yorkshire and Humber (Jones *et al*., 2007).

There is a lack of reliable data on the prevalence of alcohol dependence since UK general population surveys do not include questionnaires that provide a reliable ICD-10 diagnosis of alcohol dependence (e.g. the WHO Composite International Diagnostic Interview). Instead the most reliable estimate of alcohol dependence comes from the Psychiatric Morbidity Survey, which used a WHO measure of alcohol use disorders: the Alcohol Use Disorders Identification Test. A score of 16 or more on this questionnaire is indicative of alcohol dependence (Drummond *et al*., 2005). The Alcohol Needs Assessment Project in England found the prevalence of alcohol dependence to be 4% in 16-64 year old adults: 6% of men and 2% of women (Drummond *et al*., 2005). This equates to a population of 1.1 million people in England with alcohol dependence. There was considerable regional variation in the prevalence of alcohol dependence from 2% in East Midlands to 5% in the North West. The prevalence of hazardous and harmful drinking and dependence are highest in 16-24 year olds and decrease steadily with age. Hazardous and harmful drinking is 1.6 times greater in the white population than in the black and ethnic minority population. However, alcohol dependence is approximately equally prevalent in these two populations.

While the Government and Royal Colleges' definitions of harmful drinking and risk levels of alcohol consumption provide useful benchmarks to estimate prevalence of alcohol use disorders in the general population and monitor trends over time, they have a number of limitations. This is particularly apparent when examining an individual's risk of alcohol related harm at a given level of alcohol consumption.

According to the WHO alcohol is implicated as a risk factor in over 60 health disorders, including high blood pressure, stroke, coronary heart disease, liver cirrhosis and various cancers. The extent to which these disorders are attributable to alcohol varies. This is known as the Alcohol Attributable Fraction (AAF). The AAF for alcoholic liver disease and alcohol poisoning is 1 (or 100% alcohol attributable) (WHO, 2000). For other diseases such as cancer and heart disease the AAF is less than 1 (i.e. partly attributable to alcohol). Further, the AAF varies with age and gender. Also as noted earlier the risk with increasing levels of alcohol consumption is different for different disorders. Risk of a given level of alcohol consumption is also related to body weight, nutritional status, concurrent use of a range of medications, mental health status, contextual factors, and social deprivation, amongst other factors. Therefore it is impossible to define a level at which alcohol is universally without risk of harm.

2.3.2 Mental health

Alcohol is strongly associated with a wide range of mental health problems. Depression, anxiety, drug misuse, nicotine dependence, and self harm are commonly associated with excessive alcohol consumption. Up to 41% of suicides are attributable to alcohol and 23% of people who engage in deliberate self harm are alcohol dependent (Prime Minister's Strategy Unit, 2003). Amongst adults admitted to inpatient mental health services hazardous and harmful alcohol use increased the risk of a suicidal presentation by a factor of three, and alcohol dependence, increased the risk by a factor of eight (McCloud *et al*., 2004). In the same study 49% of patients admitted were hazardous and harmful drinkers, including 53% of men and 44% of women, and 22% of the total population were alcohol dependent (Barnaby *et al*., 2003). These prevalence rates are considerably higher than the general population, particularly in women.

A UK study found 26% of community mental health team patients were hazardous and harmful drinkers and 9% were alcohol dependent (Weaver *et al*., 2003). In the same study, examining patients attending specialist alcohol treatment services, overall 85% had a psychiatric disorder in addition to alcohol dependence. Eighty one percent had an affective and/or anxiety disorder (severe depression, 34%; mild depression, 47%, anxiety, 32%), 53% had a personality disorder, and 19% had a psychotic disorder.

2.3.3 Social problems

Alcohol is implicated in relationship breakdown, domestic violence and poor parenting, including child neglect and abuse. It is estimated that over 1 million children are affected by parental alcohol misuse, and up to 60% of child protection cases involve alcohol (Prime Minister's Strategy Unit, 2003). Alcohol also contributes to unsafe sex and unplanned pregnancy, financial problems and homelessness. Half of homeless people are alcohol dependent (Gill *et al*., 1996).

In terms of productivity, alcohol contributes to absenteeism, accidents in the workplace and decline in work performance. Up to 17 million working days are lost annually in the UK due to alcohol related absences and 58,000 working years are lost annually due to premature deaths related to alcohol (Prime Minister's Strategy Unit, 2003). Alcohol misuse can also lead to job loss, and over 38,000 people of working age in England were claiming Invalidity Benefit with a diagnosis of 'alcoholism', nearly 2% of all claimants (Deacon *et al*., 2007).

2.3.4 Criminality

Over 512,000 recorded crimes in England were attributable to alcohol in 2006 in the British Crime Survey, accounting for nearly half of all violent crimes (Walker *et al*., 2006). Nearly half of all offences of criminal damage are alcohol related, and alcohol is implicated in domestic violence, sexual assaults, burglary, theft, robbery and murder (Prime Minister's Strategy Unit, 2003). Drunk driving accounts for 5% of road accidents and around 500 death per annum, and harmful drinkers are six times more likely to be involved in a road accident (Prime Minister's Strategy Unit, 2003).

Approximately two thirds of male prisoners and over a third of female prisoners are hazardous or harmful drinkers and 70% of probation clients are hazardous or harmful drinkers (Singleton *et al*., 1998).

2.3.5 Public health impact

The WHO has estimated the global burden of disease due to alcohol using Alcohol Attributable Fractions, as described above, and found that alcohol accounts for 4% of all disease burden world wide (Rehm *et al*., 2004). Alcohol is the third leading cause of disability in the developed world after smoking and hypertension. Using the same methodology, nearly 15,000 deaths in England are caused by alcohol per annum, 3% of all deaths (Jones *et al*., 2008). Men had more than double the risk of alcohol attributable deaths compared to women, and the 16-24 year old age group had 19 times the risk of alcohol related mortality compared to those aged 75 and over (27% of all deaths in 16-24 year olds, mostly due to acute effects of alcohol: intentional self harm and road traffic accidents). In those over 35 years, deaths are more commonly due to chronic physical illness from alcohol, e.g. alcoholic liver disease, malignant cancers of the oesophagus and breast, and hypertension.

The health consequences of alcohol, including deaths from alcoholic liver disease, have been increasing in the UK compared to a reduction in many other European countries (Leon & McCambridge, 2006). Further the age at which deaths from alcoholic liver disease occur has been falling in the UK, which is partly attributable to increasing alcohol consumption in young people (ONS, 2003).

Alcohol related hospital admissions in England increased by 75% between 2002/03 and 2006/07 (NAO, 2008). For conditions directly attributable to alcohol, admissions doubled between 1996 and 2007. In 2006/07 there were 811,443 hospital admissions in England where alcohol was either a primary or secondary diagnosis (NAO, 2008). Alcohol related admissions increase steeply with age, peaking in the 45-64 year old age group (Deacon *et al*., 2007).

Forty percent of admissions to accident and emergency (A&E) departments are alcohol related, and at peak times (midnight to 5 am at weekends) this rises to 70% (Drummond *et al*., 2005). Harmful and dependent drinkers are much more likely to be frequent A&E attenders, attending on average five times per annum. Between 20% and 30% of medical admissions, and one third of primary care attendances are alcohol related (Kouimtsidis *et al*., 2003; RCP, 2001; Coulton *et al*., 2006). Further, people with alcohol dependence are twice as likely as moderate drinkers to visit their GP (Fuller *et al*., 2009).

2.4 Aetiology

There is no single factor which accounts for the variation in individual risk of developing alcohol use disorders. The evidence suggests that harmful alcohol use and alcohol dependence have a wide range of causal factors, some of which interact with each other to increase risk.

2.4.1 Family history

It is well established that alcohol dependence runs in families. In general, offspring of parents with alcohol dependence are four times more likely to develop alcohol dependence. Evidence from genetic studies, particularly those in twins, has clearly demonstrated a genetic component to the risk of alcohol dependence. A meta-analysis of 9,897 twin pairs from Australian and US studies found the heritability of alcohol dependence in excess of 50% (Goldman *et al*., 2005). However, a meta-analysis of 50 family, twin and adoption studies showed the heritability of alcohol

misuse to be at most 30-36% (Walters, 2002). Whatever the true heritability, these studies indicate that genetic factors may explain only part of the aetiology of alcohol dependence. The remaining variation is accounted for environmental factors and their interaction with genetic factors. While no single gene for alcohol dependence has so far been identified, a range of genes which determine brain function have been implicated (Agrawal *et al*., 2008).

2.4.2 Psychological factors

There is good evidence that a range of psychological factors contribute to the risk of developing alcohol use disorders. Various learning theories have provided evidence of an important role of learning in alcohol dependence. Conditioning theories provide an explanation for the development of alcohol dependence. Alcohol, being a psychoactive drug, has reinforcing properties, for example through its pleasurable effects, and its ability to relieve negative mood states such as anxiety. Conditioning can also explain why people become particularly sensitive to stimuli or cues associated with alcohol consumption, for example, the sight and smell of a favourite drink, such that these cues can trigger craving for and continued use of alcohol, including relapse after a period of abstinence (Drummond *et al*., 1990).

Social learning theory also provides some explanations of increased risk of excessive drinking and the development of alcohol dependence. People can learn from families and peer groups through a process of modelling patterns of drinking and expectancies (beliefs) about the effects of alcohol. Teenagers with higher positive expectancies (for example, that drinking is pleasurable and desirable) are more likely to start drinking at an earlier age and to drink more heavily (Christiansen *et al*., 1989; Dunn & Goldman, 1998).

2.4.3 Personality factors

The idea that a particular 'addictive personality' leads to the development of alcohol dependence is popular with many addiction counsellors, but does not have strong support from research. Often with patients in treatment for alcohol dependence it is difficult to disentangle the effects of alcohol on the expression of personality and behaviour, from those personality factors which preceded alcohol dependence. Nevertheless people with alcohol dependence have a 21 fold higher risk of also having antisocial personality disorder (ASPD; Regier *et al*., 1990), and people with ASPD have a higher risk of severe alcohol dependence (Goldstein *et al*., 2007). Recent evidence points to the importance of disinhibition traits, such as novelty and sensation seeking, poor impulse control, as factors related to increased risk of both alcohol and drug dependence, which may have a basis in abnormal brain function in the pre-frontal cortex (Kalivas & Volkow, 2005; Dick *et al*., 2007).

2.4.4 Psychiatric comorbidity

As noted earlier people with alcohol dependence have higher rates of comorbidity with other psychiatric disorders than people in the general population, particularly depression, anxiety, post traumatic stress disorder, psychosis, and drug misuse. Alcohol can, temporarily at least, reduce the symptoms of anxiety and depression, leading to the theory that alcohol use in this situation is a form of 'self medication'. This theory however lacks clear experimental support, and the longer term effects of alcohol are to increase these disorders.

2.4.5 Stress, adverse life events and abuse

There is clear evidence that adverse life events can trigger excessive drinking, and may predispose to the development of alcohol dependence. This is particularly apparent in alcohol dependence developing later in life following, for example, a bereavement or job loss. Stressful life situations or events can also trigger heavy drinking. People with alcohol dependence also report much higher levels of childhood abuse and neglect, particularly sexual abuse. One UK study found 54% of female and 24% of male alcohol dependent patients identified themselves as victims of sexual abuse, mostly before the age of 16 (Moncrieff *et al*., 1996). Further they were more likely to have a family history of alcohol misuse, and began drinking and developed alcohol dependence earlier than those without such a history.

2.4.6 Other environmental and cultural factors

There is a wide range of other environmental factors which predispose to the development of alcohol use disorders (Cook, 1994). These include the affordability and availability of alcohol, high consumption rates in the general population, occupational risk factors (such as working in the alcohol industry), social pressure to drink, and religious and culturally related attitudes towards alcohol.

2.5 Course of harmful alcohol use and dependence

Harmful alcohol use and dependence are relatively uncommon before the age of 15, but increase steeply to reach a peak in the early twenties, this being the period when alcohol use disorders are most likely to begin. One US general population study found the prevalence of alcohol dependence to be 2% in 12-17 year olds, rising to 12% in 18-20 year olds (Grant *et al*., 2004). Thereafter the prevalence of alcohol use disorders declines steadily with age. The same US study found the prevalence of dependence was 4% in 30-34 year olds and 1.5% in 50-54 year olds. A similar UK study found the prevalence of alcohol dependence to be 6% in 16-19 year olds, 8.2% in 20-24 year olds, 3.6% in 30-34 year olds, and 2.3% in 50-54 year olds (Drummond *et al*., 2005). Therefore it is clear that there is substantial remission from alcohol use disorders over time. Much of this remission takes place without contact with alcohol treatment services (Dawson *et al*., 2005).

However, it is also known that people who develop alcohol dependence at a younger age tend to have a more chronic course (Dawson *et al*., 2008). Further, while a large proportion of those who meet the criteria for alcohol dependence in their twenties will remit over the following two decades; those who remain alcohol dependent in their forties will tend to have a more chronic course. This is the typical age group of people entering specialist alcohol treatment. Most studies examining the outcome of people attending alcohol treatment find that 70-80% will relapse in the year following treatment, with the highest rate of relapse taking place in the first three months after completing treatment (Hunt *et al*., 1971). Those who remain abstinent from alcohol for the first year after treatment have a relatively low risk of relapse thereafter. Factors associated with a worse outcome include having less social stability and support (for example, those without jobs or families or stable housing), lacking a social network of non-drinkers, a family history of alcohol dependence, psychiatric comorbidity, multiple previous treatment episodes, and history of disengagement from treatment.

In contrast with the positive prognosis in younger people with alcohol dependence in the general population, the longer term prognosis of alcohol dependence for people entering specialist treatment is relatively poor. Over a 20 year period about one third have continuing alcohol problems, a third show some improvement, and a third have a good outcome (either abstinence or moderate drinking). The mortality rate is high in this population, nearly four times the age adjusted rate for people without alcohol dependence. Those who are more severely alcohol dependent are less likely to achieve lasting stable moderate drinking, and have a higher mortality than those who are less dependent. It is important to note that most of the excess mortality is largely accounted for by lung cancer and heart disease which are strongly related to continued tobacco smoking.

2.6 Pharmacology of alcohol

Following ingestion, alcohol is rapidly absorbed by the gut and enters the bloodstream with a peak in blood alcohol concentration after 30 to 60 minutes. Alcohol is then distributed around every part of the body. It readily crosses the blood-brain barrier to enter the brain where it causes subjective or psychoactive and behavioural effects, and following high levels of chronic alcohol intake, it can cause cognitive impairment and brain damage.

Alcohol is excreted in urine, sweat and breath, but the main method of elimination from the body is by metabolism in the liver, where it is converted to acetaldehyde and acetate. These metabolites are then excreted from the body primarily in urine. The rate at which alcohol is metabolised and the extent to which an individual is affected by a given dose of alcohol is highly variable from one individual to another. These individual differences affect drinking behaviour and the potential for alcohol related harm and alcohol dependence. Also the effects of alcohol vary in the same individual over time, depending on several factors including whether food has been consumed, rate of drinking, nutritional status, environmental context, and concurrent use of other psychoactive drugs. Therefore it is very difficult to predict the effects of a given amount of alcohol both between individuals and within individuals over time. For instance clinically the impact on the liver varies so that some suffer liver failure early on in their drinking whilst in others drinking heavily, liver function is relatively normal.

Alcohol is a toxic substance and its toxicity is related to the quantity and duration of alcohol consumption. It can have toxic effects on every organ in the body. In the brain, in a single drinking episode, increasing levels of alcohol lead initially to stimulation, experienced as pleasure, excitement, talkativeness. At increasing concentrations it causes sedation leading to sensations of relaxation, later to slurred speech, unsteadiness, loss of coordination, incontinence, coma, and ultimately death through alcohol poisoning due to sedation of vital brain functions on breathing and circulation.

The dependence producing properties of alcohol have been studied extensively in the last 20 years. Alcohol affects a wide range of neurotransmitter systems in the brain leading to the features of alcohol dependence. The main neurotransmitter systems affected by alcohol are GABA, glutamate, dopamine, and opioid (Nutt, 1999). The action of alcohol on GABA is similar to the effects of other sedatives such as benzodiazepines, and is responsible for alcohol's sedating and anxiolytic

properties (Krystal *et al*., 2006). Glutamate is a major neurotransmitter responsible for brain stimulation and alcohol affects glutamate through its inhibitory action on NMDA-type glutamate receptors, producing amnesia, for example, blackouts and sedation (Krystal *et al*., 1999).

Chronic alcohol consumption leads to the development of tolerance through a process of neuroadaptation: receptors in the brain gradually adapt to the effects of alcohol to compensate for stimulation or sedation. This is experienced by the individual as the same amount of alcohol having less effect over time. This can lead to an individual increasing alcohol consumption to achieve the desired psychoactive effects. The key neurotransmitters involved in tolerance are GABA and glutamate, with chronic alcohol intake associated with reduced GABA inhibitory function and increased NMDA-glutamatergic activity (Krystal *et al*., 2003; 2006). This GABA-glutamate imbalance is acceptable in the presence of alcohol which increases GABA and reduces NMDA-glutamate activity. However, when the alcohol dependent individual stops drinking, the imbalance between these neurotransmitter systems now results in the brain becoming overactive after a few hours, leading to unpleasant withdrawal symptoms such as anxiety, sweating, craving, fits and hallucinations. This can be life threatening in severe cases and requires urgent medical treatment. Repeated withdrawal is also thought to underlie the toxic effect of alcohol on neurons leading to cognitive impairment and brain damage (Loeber *et al*, 2009). The effects of alcohol withdrawal can take up to between three months and a year to fully recover: referred to as the protracted withdrawal syndrome. Even then the brain remains abnormally sensitive to alcohol, and when drinking is resumed, tolerance and withdrawal can return within a few days: known as reinstatement. This makes it extremely difficult for a person who has developed alcohol dependence to return to sustained moderate drinking.

The brain's endogenous opioid system is also affected by alcohol (Oswald & Wand, 2004). Alcohol stimulates endogenous opioids, which is thought to be related to the pleasurable, reinforcing effects of alcohol. Opioids in turn stimulate the dopamine system in the brain which is thought to be responsible for appetite for a range of appetitive behaviours including regulation of appetite for food, sex and psychoactive drugs. The dopamine system is also activated by stimulant drugs such as amphetamines and cocaine, and it is through this process that the individual seeks more drugs or alcohol (Robinson & Berridge, 2008; Everitt *et al*, 2008). There is evidence that drugs that block the opioid neurotransmitters, such as naltrexone, can reduce the reinforcing or pleasurable properties of alcohol and so reduce relapse in alcohol dependent patients (Anton, 2008).

2.7 Identification and diagnosis

People with alcohol use disorders commonly present to health, social and criminal justice agencies, often with problems associated with their alcohol use, but they less often seek help specifically for the alcohol problem itself. Further, alcohol use disorders are seldom identified by health and social care professionals. One recent study found that UK general practitioners routinely identify only a small proportion of people with alcohol use disorders who present to primary care (<2% of hazardous or harmful drinkers; <5% of alcohol dependent drinkers) (Cheeta *et al*., 2008). This has important implications for prevention and treatment of alcohol use disorders. Failure to identify alcohol use disorders means that many people are denied access to

alcohol interventions until the problems are more chronic and difficult to treat. Further, failure to address an underlying alcohol problem may undermine the effectiveness of treatment for the presenting health problem (e.g. depression or high blood pressure).

Screening and brief intervention delivered by a non-specialist practitioner is a cost effective approach for hazardous and harmful drinkers (NICE, 2010a). However for people with alcohol dependence brief interventions are less effective, and referral to a specialist service is likely to be necessary (Miller & Wilbourne, 2002). It is important therefore that health and social care professionals are able to identify and appropriately refer harmful drinkers who do not respond to brief intervention, and those with alcohol dependence, to appropriate specialist services.

Around a third of people presenting to specialist alcohol services in England are self referred, and approximately one third are referred by non-specialist health or social care professionals (Drummond *et al.*, 2005). The remainder are referred by other specialist addiction services. At the point of entry to treatment it is essential that patients are appropriately diagnosed and assessed in order to decide on the most appropriate treatment and management, assess the level of risk, such as self harm, risks to others, and identify co-occuring problems that may need particular attention, for example psychiatric comorbidity, physical illness, problems with housing, vulnerability, pregnancy (NTA, 2006). Therefore assessment should not be narrowly focused on alcohol consumption, but should include all areas of physical, psychological and social functioning.

Since alcohol dependence is associated with a higher level of problems, a more chronic course, and requires a higher level of medical and psychiatric intervention, it is essential that practitioners in specialist alcohol services are able to appropriately diagnose and assess alcohol dependence.

2.8 The role of treatment and management

As noted above, many people will recover from alcohol use disorders without specialist treatment, and many will reduce their alcohol intake following a change in circumstances, such as parenthood, marriage, taking on a responsible job. Hazardous and harmful drinkers, may respond to a brief intervention provided in primary care without requiring access to specialist treatment (NICE, 2010a). For others, their alcohol problems are overcome with the help of a mutual aid organisation, such as Alcoholics Anonymous (see section 1.10). Nevertheless, many will require access to specialist treatment by virtue of having more severe or chronic alcohol problems, or a higher level of complications of their drinking (e.g. social isolation, psychiatric comorbidity, severe alcohol withdrawal).

The primary role of specialist treatment is to assist the individual to reduce or stop drinking alcohol in a safe manner (NTA, 2006). At the initial stages of engagement with specialist services, service users may be ambivalent about changing their drinking behaviour or dealing with their problems. At this stage work on enhancing the patient's motivation towards making changes and engagement with treatment will be particularly important.

For most people with alcohol dependence the most appropriate goal in terms of alcohol consumption should be to aim for complete abstinence. With an increasing level of alcohol dependence a return to moderate or 'controlled' drinking becomes increasingly difficult (Edwards & Gross, 1976; Schuckit, 2009). Further, for alcohol misusers with significant psychiatric or physical comorbidity (e.g. depressive disorder or alcoholic liver disease), abstinence is the appropriate goal. However, hazardous and harmful drinkers and those with a low level of alcohol dependence may be able to achieve a goal of moderate alcohol consumption (Raistrick *et al*., 2006). Where a client has a goal of moderation but the clinician believes there are considerable risks in doing so, the clinician should provide strong advice that abstinence is most appropriate, but should not deny the client treatment if the advice is unheeded (Raistrick *et al*., 2006)

For people with alcohol dependence the next stage of treatment may require medically assisted alcohol withdrawal, if necessary with medication to control the symptoms and complications of withdrawal. For people with severe alcohol dependence and/or significant physical or psychiatric comorbidity, this may require assisted alcohol withdrawal in an inpatient or residential setting, such as a specialist NHS inpatient addiction treatment unit (SCAN, 2006). For the majority, however, alcohol withdrawal can be managed in the community either as part of shared care with the patient's general practitioner or in an outpatient or home based assisted alcohol withdrawal programme, with appropriate professional and family support (Raistrick *et al,* 2006). Treatment of alcohol withdrawal is, however, only the beginning of rehabilitation and for many, a necessary precursor to a longer term treatment process. Withdrawal management should therefore not be seen as a stand alone treatment.

People with alcohol dependence who have recently stopped drinking are vulnerable to relapse, and often have many unresolved co-occurring problems which predispose to relapse (e.g. psychiatric comorbidity, social problems) (Marlatt & Gordon, 1985). In this phase, the primary role of treatment is the prevention of relapse. This should include interventions aimed primarily at the drinking behaviour, including psychosocial and pharmacological interventions, and interventions aimed at dealing with co-occurring problems. Interventions aimed to prevent relapse include individual therapy (for example, motivational enhancement therapy, cognitive behaviour therapy), group and family based therapies, community based and residential rehabilitation programmes, medications to attenuate drinking or promote abstinence (for example, naltrexone, acamprosate, disulfiram), and interventions promoting social support and integration (for example, social behavioural network therapy, twelve step facilitation) (Raistrick *et al*, 2006).

Although psychiatric comorbidity is common in people seeking help for alcohol use disorders, this will usually resolve within a few weeks of abstinence from alcohol without formal psychiatric intervention (Petrakis *et al*, 2002). However, a proportion of people with psychiatric comorbidity, usually those in whom the mental disorder preceded alcohol dependence, will require psychosocial or pharmacological interventions specifically for the comorbidity. Self harm and suicide are relatively common in people with alcohol dependence (Sher, 2006). Therefore, treatment staff need to be trained to identify, monitor, and if necessary treat or refer to an appropriate mental health specialist, those patients with comorbidity which persists beyond the withdrawal period, and/or are at risk of self harm or suicide. Patients

with complex psychological issues related to trauma, sexual abuse or bereavement will require specific interventions delivered by appropriately trained personnel (Raistrick *et al.*, 2006).

Often people with alcohol dependence, particularly in the immediate post-withdrawal period, find it difficult to cope with typical life challenges such as managing their finances or dealing with relationships. They will therefore require additional support directed at these areas of social functioning. Specific social problems such as homelessness, isolation, marital breakdown, child care issues including parenting problems, child abuse and neglect, will require referral to, and liaison with, appropriate social care services (NTA, 2006). A proportion of patients entering specialist treatment are involved with the criminal justice system, and some may be entering treatment as a condition of a Court order. Therefore appropriate liaison with criminal justice services is essential for this group.

People with alcohol dependence are often unable to take care of their health during drinking periods, and are at high risk of developing a wide range of health problems due to their drinking (Rehm *et al.*, 2003). Treatment staff therefore need to be able to identify and assess physical health consequences of alcohol use, and refer patients to appropriate medical services.

In the later stages of treatment the focus will be more on reintegration into society and restoration of normal function, including establishing a healthy lifestyle, finding stable housing, re-entering employment, re-establishing contact with their families, and forming appropriate and fulfilling relationships (NTA, 2006). All of these factors are important in promoting longer term stable recovery.

2.9 Current care in the NHS

A recent alcohol needs assessment in England identified nearly 700 agencies providing specialist alcohol treatment, with an estimated workforce of 4,250 and an annual spend of around £217 millions (Drummond *et al*., 2005). The majority of agencies (70%) were community based and the remainder were residential, including inpatient units in the NHS, and residential rehabilitation programmes mainly provided by the non-statutory or private sector. Overall approximately half of all alcohol services are provided by the non-statutory sector, but are typically funded by the NHS or local authorities. Approximately a third of specialist alcohol services exclusively provide treatment for people with alcohol problems, but the majority (58%) provide services for both drug and alcohol misusers.

In terms of services provided by community specialist agencies, the majority (63%) provide structured psychological interventions either on an individual basis or as part of a structured community programme (Drummond *et al*., 2005). Only 30% provide some form of assisted alcohol withdrawal programme, and few (<20%) provide medications for relapse prevention. Of the residential programmes, 45% provide inpatient medically assisted alcohol withdrawal and 60% provide residential rehabilitation. The rehabilitation programmes are typically of 3-6 months duration and the alcohol withdrawal programmes are typically of 2-3 weeks duration.

It is estimated that approximately 63,000 people entered specialist treatment for alcohol use disorders in 2003-04 (Drummond *et al*., 2005). The recently established

National Alcohol Treatment Monitoring System (NATMS) reported 104,000 people entering 1,464 agencies in 2008-09, of whom 70,000 were new presentations (NTA, 2009). However it is not possible to identify what proportion of these patients are primarily alcohol dependent and what proportion of services are being provided by primary care under the Enhanced Care provision.

However the 2004 alcohol needs assessment found that only 1 out of 18 people with alcohol dependence in the general population accesses treatment per annum (Drummond *et al*., 2005). Access varies considerably from 1 in 12 in the North West Region to 1 in 102 in the North East. A low level of access to treatment is regarded as 1 in 10 (Rush, 1990). A recent Scottish national alcohol needs assessment using the same methods found treatment access to be higher, than in England with 1 in 12 accessing treatment per annum. This level of access may have improved in England since 2004 based on the NATMS data. However, the National Audit Office (2008) reported that the spending on specialist alcohol services by Primary Care Trusts was not based on a clear understanding of the level of need in different parts of England. There is therefore some way to go in making alcohol treatment accessible throughout England.

2.10 Service user organisations

There are several organisations available in England to provide mutual aid for service users and their families. The largest and longest established such organisation is Alcoholics Anonymous (AA). Founded in the US in the 1930s, AA is based on a '12 step' programme, and the 'twelve traditions' of AA. The programme includes acceptance that one is powerless over alcohol, acceptance of the role of a higher power, and the role of the support of other members. AA is self financing, and the seventh tradition is that AA groups should decline outside contributions. In 2009, AA membership worldwide was reported as nearly 2 million (AA, 2009). While AA might not suit all alcohol misusers, its advantages include its wide availability and open access.

Allied to AA is Al-anon and Alateen, jointly known as Al-anon Family Groups. Al-anon uses the same twelve steps as AA with some modifications and is focused on meeting the needs of friends and family members of alcoholics. Again meetings are widely available and provide helpful support beyond what can be provided by specialist treatment services.

Another organisation developing England is SMART (Self-Management and Recovery Training). Its development is being supported by Alcohol Concern, a leading UK alcohol charity, and the Department of Health. SMART is another mutual aid organisation but is based more on cognitive behavioural principles and provides an alternative to AA (see www.smartrecovery.org).

2.11 Impact on families

The adverse effects of alcohol dependence on family members are considerable. Marriages where one or both partners have an alcohol problem are twice as likely to end in divorce as those in which alcohol is not a problem. Nearly a million children live with one or more parents who are alcohol misusers and 6% of adults report having grown up in such a family. Alcohol is implicated in a high proportion of cases

of child neglect and abuse, and heavy drinking was identified as a factor in 50% of child protection cases (Orford *et al.,* 2005)

Partners of people with harmful alcohol use and dependence experience higher rates of domestic violence than where alcohol misuse is not a feature. Some 70% of men who assault their partners do so under the influence of alcohol (Murphy *et al*, 2005). Family members of people with alcohol dependence have high rates of psychiatric morbidity, and growing up with an alcohol misuser increases the likelihood of teenagers taking up alcohol early and developing alcohol problems themselves (Latendresse *et al*., 2010).

All of this points to the importance of addressing the needs of family members of alcohol misusers. This includes the need for specialist treatment services to assess the impact of the individual's drinking on family members, and the need to ensure the safety of children living with alcohol misusers.

2.12 Economic impact

The alcohol misuse and the problems related to present a considerable cost to society. Estimates of the economic costs attempt to assess in monetary terms the damage that results from the misuse of alcohol. These costs include expenditures on alcohol-related problems and opportunities that are lost because of alcohol (NIAAA, 1991).

Many challenges exist in estimating the costs required for cost-of-illness studies in health, there are two such challenges that are particularly relevant to the case of alcohol abuse. First, researchers attempt to identify costs that are caused by, and not merely associated with, alcohol misuse, yet it is often hard to establish causation (Cook, 1990; NIAAA, 1991). Second, many costs resulting from alcohol abuse cannot be measured directly. This is especially true of costs that involve placing a value on lost productivity. Researchers use mathematical and statistical methods to estimate such costs, yet recognize that this is imprecise. Moreover, costs of pain and suffering of both people who misuse alcohol and people affected by them cannot be estimated in a reliable way, and are therefore not considered in most cost studies. These challenges highlight the fact that although the economic cost of alcohol misuse can be estimated, it cannot be measured precisely. Nevertheless, estimates of the cost give us an idea of the dimensions of the problem, and the breakdown of costs suggests to us which categories are most costly (NIAAA, 1991).

The first category of costs is that of treating the medical consequences of alcohol misuse and treating alcohol misuse. The second category of health-related costs includes losses in productivity by workers who misuse alcohol. The third category of health-related costs is the loss to society because of premature deaths due to alcohol misuse. In addition to the health-related costs of alcohol misuse are costs involving the criminal justice system, social care, property losses from alcohol-related motor vehicle crashes and fires, and lost productivity of the victims of alcohol-related crime and individuals imprisoned as a consequence of alcohol-related crime (NIAAA, 1991).

The UK Cabinet Office recently estimated that the cost of alcohol to society was £25.1 billions per annum (Department of Health, 2007). This includes costs to the NHS of

£1.7 billions. Accident and emergency departments and ambulance services account for 30% of these costs, and acute hospitals, 56% of costs, through admissions and outpatient attendances (NAO, 2008). However, specialist alcohol treatment services account for only 2% of total costs. Crime and disorder costs amount to £7.3 billions, including costs for policing, drink driving, courts and the criminal justice system, and costs to services both in anticipation, and in dealing with the consequences, of alcohol related crime (Prime Minister's Strategy Unit, 2003). The estimated costs in the workplace amount to some £6.4 billions through lost productivity, absenteeism, alcohol-related sickness and premature deaths (Prime Minister's Strategy Unit, 2003).

For the EU, US and Canada social costs of alcohol were estimated to be around €270bn (2003 prices) (Anderson and Baumberg, 2005), USA$185bn (1998 prices) (WHO, 2004), and CAN$14.6bn (2002 prices) (Rhem *et al.,* 2006), respectively.

3. Methods used to develop this guideline

3.1 Overview

The development of this guideline drew upon methods outlined by NICE (further information is available in *The Guidelines Manual* [NICE, 2009]). A team of health professionals, lay representatives and technical experts known as the Guideline Development Group (GDG), with support from the NCCMH staff, undertook the development of a patient centred, evidence-based guideline. There are six basic steps in the process of developing a guideline:

- Define the scope, which sets the parameters of the guideline and provides a focus and steer for the development work.
- Define review questions considered important for practitioners and service users.
- Develop criteria for evidence searching and search for evidence.
- Design validated protocols for systematic review and apply to evidence recovered by search.
- Synthesise and (meta-) analyse data retrieved, guided by the review questions, and produce GRADE evidence profiles and summaries.
- Answer review questions with evidence-based recommendations for clinical practice.

The clinical practice recommendations made by the GDG are therefore derived from the most up-to-date and robust evidence base for the clinical and cost effectiveness of the treatments and services used in the treatment and management of alcohol dependence and harmful alcohol use. In addition, to ensure a service user and carer focus, the concerns of service users and carers regarding health and social care have been highlighted and addressed by recommendations agreed by the whole GDG.

3.2 The scope

Guideline topics are selected by the Department of Health and the Welsh Assembly Government, which identify the main areas to be covered by the guideline in a specific remit (see *The Guidelines Manual* for further information). The NCCMH developed a scope for the guideline based on the remit.

The purpose of the scope is to:

- provide an overview of what the guideline will include and exclude
- identify the key aspects of care that must be included
- set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC and the remit from the Department of Health/Welsh Assembly Government

- inform the development of the review questions and search strategy
- inform professionals and the public about expected content of the guideline

keep the guideline to a reasonable size to ensure that its development can be carried out within the allocated period.

The draft scope was subject to consultation with registered stakeholders over a 4-week period. During the consultation period, the scope was posted on the NICE website (www.nice.org.uk). Comments were invited from stakeholder organisations and the Guideline Review Panel (GRP). Further information about the GRP can also be found on the NICE website. The NCCMH and NICE reviewed the scope in light of comments received, and the revised scope was signed off by the GRP.

3.2.1 The guideline development group

The GDG consisted of: professionals in psychiatry, clinical psychology, nursing, social work, and general practice; academic experts in psychiatry and psychology; and service user, lay member and carer representatives. The guideline development process was supported by staff from the NCCMH, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process, and contributed to drafting the guideline.

3.2.2 Guideline Development Group meetings

Twelve GDG meetings were held between March 2009 and May 2010. During each day-long GDG meeting, in a plenary session, review questions and clinical and economic evidence were reviewed and assessed, and recommendations formulated. At each meeting, all GDG members declared any potential conflicts of interest, and service user and carer concerns were routinely discussed as part of a standing agenda.

3.2.3 Topic groups

The GDG divided its workload along clinically relevant lines to simplify the guideline development process, and GDG members formed smaller topic groups to undertake guideline work in that area of clinical practice. Topic Group 1 covered questions relating to pharmacological intervention. Topic Group 2 covered psychological and psychosocial interventions. Topic Group 3 covered assessment of alcohol misuse, Topic Group 4 covered service user and carer experiences of care, and Topic Group 5 covered delivery settings for treatment. . These groups were designed to efficiently manage the large volume of evidence appraisal prior to presenting it to the GDG as a whole. Each topic group was chaired by a GDG member with expert knowledge of the topic area (one of the healthcare professionals). Topic groups refined the review questions, refined the clinical definitions of treatment interventions, reviewed and prepared the evidence with the systematic reviewer before presenting it to the GDG as a whole and helped the GDG to identify further expertise in the topic. Topic group leaders reported the status of the group's work as part of the standing agenda. They also introduced and led the GDG discussion of the evidence review for that topic and assisted the GDG Chair in drafting the section of the guideline relevant to the work of each topic group.

3.2.4 Service users and carers

Individuals with direct experience of services gave an integral service-user focus to the GDG and the guideline. The GDG included service user, carer and lay representatives who contributed as full GDG members to writing the review questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline, and bringing service-user research to the attention of the GDG. In drafting the guideline, they contributed to writing the guideline's experience of care chapter and identified recommendations from the service user and carer perspective.

3.2.5 Special advisors

Special advisors, who had specific expertise in one or more aspects of treatment and management relevant to the guideline, assisted the GDG, commenting on specific aspects of the developing guideline and making presentations to the GDG. Appendix 3 lists those who agreed to act as special advisors.

3.2.6 National and international experts

National and international experts in the area under review were identified through the literature search and through the experience of the GDG members. These experts were contacted to recommend unpublished or soon-to-be published studies in order to ensure up-to-date evidence was included in the development of the guideline. They informed the group about completed trials at the pre-publication stage, systematic reviews in the process of being published, studies relating to the cost effectiveness of treatment and trial data if the GDG could be provided with full access to the complete trial report. Appendix 6 lists researchers who were contacted.

3.2.7 Integration of other guidelines on alcohol-use disorders

In addition to this guideline, there are two other pieces of NICE guidance addressing alcohol-use disorders outlined in Chapter 1. During development steering group meetings have been held, in which representatives from the three development groups meet to discuss any issues, such as overlapping areas of review work and integration of the guidelines.

Review (clinical) questions were used to guide the identification and interrogation of the evidence base relevant to the topic of the guideline. Before the first GDG meeting, an analytic framework (see Appendix 7) was prepared by NCCMH staff based on the scope and an overview of existing guidelines, and discussed with the guideline Chair. The framework was used to provide a structure from which the review questions were drafted. Both the analytic framework and the draft review questions were then discussed by the GDG at the first few meetings and amended as necessary. Where appropriate, the framework and questions were refined once the evidence had been searched and, where necessary, sub-questions were generated. Questions submitted by stakeholders were also discussed by the GDG and the rationale for not including any questions was recorded in the minutes. The final list of review questions can be found in Appendix 7.

For questions about interventions, the PICO (Patient, Intervention, Comparison and Outcome) framework was used (see Table 2).

Table 2: Features of a well-formulated question on effectiveness intervention – the PICO guide

Patients/ population	Which patients or population of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?
Intervention	Which intervention, treatment or approach should be used?
Comparison	What is/are the main alternative/s to compare with the intervention?
Outcome	What is really important for the patient? Which outcomes should be considered: intermediate or short-term measures; mortality; morbidity and treatment complications; rates of relapse; late morbidity and readmission; return to work, physical and social functioning and other measures such as quality of life; general health status; costs?

Questions relating to assessment and diagnosis do not involve an intervention designed to treat a particular condition, therefore the PICO framework was not used. Rather, the questions were designed to pick up key issues specifically relevant to diagnostic tests, for example their accuracy, reliability and safety.

In some situations, the prognosis of a particular condition is of fundamental importance, over and above its general significance in relation to specific interventions. Areas where this is particularly likely to occur relate to assessment of risk, for example in terms of behaviour modification or screening and early intervention. In addition, review questions related to issues of service delivery are occasionally specified in the remit from the Department of Health/Welsh Assembly Government. In these cases, appropriate review questions were developed to be clear and concise.

To help facilitate the literature review, a note was made of the best study design type to answer each question. There are four main types of review question of relevance to NICE guidelines. These are listed in Table 2. For each type of question, the best primary study design varies, where 'best' is interpreted as 'least likely to give misleading answers to the question'.

However, in all cases, a well-conducted systematic review (of the appropriate type of study) is likely to always yield a better answer than a single study.

Deciding on the best design type to answer a specific review question does not mean that studies of different design types addressing the same question were discarded.

Table 3: Best study design to answer each type of question

Type of question	Best primary study design
Effectiveness or other impact of an intervention	Randomised controlled trial; other studies that may be considered in the absence of RCTs are the following: internally/externally controlled before and after trial, interrupted time-series
Accuracy of information (e.g. risk factor, test, prediction rule)	Comparing the information against a valid gold standard in a randomised trial or inception cohort study
Rates (of disease, patient experience, rare side effects)	Prospecitve cohort, registry, cross-sectional study
Costs	Naturalistic prospective cost study

The GDG classified each review question into one of three groups: 1) questions concerning good practice; 2) questions likely to have little or no directly relevant evidence; and 3) questions likely to have a good evidence base. Questions concerning good practice were answered by the GDG using informal consensus. For questions that were unlikely to have a good evidence base, a brief descriptive review was initially undertaken, and then the GDG used informal consensus to reach a decision (see Section 3.5.7). For questions with a good evidence base, the review process followed the methods outlined in Section 3.5.2.

3.2.8 Clinical evidence methods

The aim of the clinical evidence review was to systematically identify and synthesise relevant evidence from the literature in order to answer the specific review questions developed by the GDG. Thus, clinical practice recommendations are evidence-based, where possible, and, if evidence is not available, informal consensus methods are used (see Section 3.5.7) and the need for future research is specified.

3.2.9 The search process

Scoping searches

A broad preliminary search of the literature was undertaken in September 2008 to obtain an overview of the issues likely to be covered by the scope, and to help define key areas. Searches were restricted to clinical guidelines, health technology assessment reports, key systematic reviews and randomised controlled trials, and conducted in the following databases and websites:

- BMJ Clinical Evidence
- Canadian Medical Association (CMA) Infobase [Canadian guidelines]
- Clinical Policy and Practice Program of the New South Wales Department of Health (Australia)
- Clinical Practice Guidelines [Australian Guidelines]
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Database of Systematic Reviews (CDSR)
- EMBASE
- Guidelines International Network (G-I-N)

- Health Evidence Bulletin Wales
- Health Management Information Consortium [HMIC]
- Health Technology Assessment (HTA) database (technology assessments)
- MEDLINE / MEDLINE in Process
- National Health and Medical Research Council (NHMRC)
- National Library for Health (NLH) Guidelines Finder
- New Zealand Guidelines Group
- NHS Centre for Reviews and Dissemination (CRD)
- OMNI Medical Search
- Scottish Intercollegiate Guidelines Network (SIGN)
- Turning Research Into Practice (TRIP)
- United States Agency for Healthcare Research and Quality (AHRQ)
- Websites of NICE and the National Institute for Health Research (NIHR) HTA Programme for guidelines and HTAs in development.

Existing NICE guidelines were updated where necessary. Other relevant guidelines were assessed for quality using the AGREE instrument (AGREE Collaboration, 2003). The evidence base underlying high-quality existing guidelines was utilised and updated as appropriate. Further information about this process can be found in The Guidelines Manual (NICE, 2009).

Systematic literature searches

After the scope was finalised, a systematic search strategy was developed to locate all the relevant evidence. The balance between sensitivity (the power to identify all studies on a particular topic) and specificity (the ability to exclude irrelevant studies from the results) was carefully considered, and a decision made to utilise a broad approach to searching to maximise retrieval of evidence to all parts of the guideline. Searches were restricted to systematic reviews, meta-analyses, randomised controlled trials, and qualitative research, and conducted in the following databases:

- AMED
- CINAHL
- EMBASE
- MEDLINE / MEDLINE In-Process
- PsycINFO
- Cochrane Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Health Technology Assessment (HTA) database

For standard mainstream bibliographic databases (AMED, CINAHL, EMBASE, MEDLINE and PsycINFO) search terms on alcohol dependence and harmful alcohol use were combined with study design filters for systematic reviews, randomised controlled trials and qualitative research. For searches generated in databases with collections of study designs at their focus (DARE, CDSR, CENTRAL and HTA) search terms on alcohol dependence and

harmful alcohol use were used without a filter. The sensitivity of this approach was aimed at minimising the risk of overlooking relevant publications, due to inaccurate or incomplete indexing of records, as well as potential weaknesses resulting from more focused search strategies (for example, for interventions).

Reference Manager

Citations from each search were downloaded into Reference Manager (a software product for managing references and formatting bibliographies) and duplicates removed. Records were then screened against the inclusion criteria of the reviews before being quality appraised (see Section 3.5.2). To keep the process both replicable and transparent, the unfiltered search results were saved and retained for future potential re-analysis.

Search filters

The search filters for systematic reviews and randomised controlled trials are adaptations of filters designed by the Centre for Reviews and Dissemination (CRD) and the Health Information Research Unit of McMaster University, Ontario. The qualitative research filter was developed in-house. Each filter comprises index terms relating to the study type(s) and associated textwords for the methodological description of the design(s).

Date and language restrictions

Systematic database searches were initially conducted in June 2008 up to the most recent searchable date. Search updates were generated on a 6-monthly basis, with the final re-runs carried out in March 2010 ahead of the guideline consultation. After this point, studies were only included if they were judged by the GDG to be exceptional (for example, if the evidence was likely to change a recommendation).
Although no language restrictions were applied at the searching stage, foreign language papers were not requested or reviewed, unless they were of particular importance to a clinical question. Date restrictions were not applied, except for searches of systematic reviews, which were limited to research published from 1993 onwards.

Other search methods

Other search methods involved: 1) scanning the reference lists of all eligible publications (systematic reviews, stakeholder evidence and included studies) for more published reports and citations of unpublished research; 2) sending lists of studies meeting the inclusion criteria to subject experts (identified through searches and the GDG) and asking them to check the lists for completeness, and to provide information of any published or unpublished research for consideration (See Appendix 3); 3) checking the tables of contents of key journals for studies that might have been missed by the database and reference list searches; 4) tracking key papers in the Science Citation Index (prospectively) over time for further useful references.

Full details of the search strategies and filters used for the systematic review of clinical evidence are provided in Appendix 9.

Study selection and quality assessment

All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility at the time they were being entered into the study information database. More specific eligibility criteria were developed for each review question and are described in the relevant clinical evidence chapters. Eligible systematic reviews and primary-level studies were critically appraised for methodological quality (see Appendix 11 for methodology checklists). The eligibility of each study was confirmed by at least one member of the appropriate topic group.

For some review questions, it was necessary to prioritise the evidence with respect to the UK context (that is, external validity). To make this process explicit, the topic groups took into account the following factors when assessing the evidence:

- participant factors (for example, gender, age and ethnicity)
- provider factors (for example, model fidelity, the conditions under which the intervention was performed and the availability of experienced staff to undertake the procedure)
- cultural factors (for example, differences in standard care and differences in the welfare system).

It was the responsibility of each topic group to decide which prioritisation factors were relevant to each review question in light of the UK context and then decide how they should modify their recommendations.

Unpublished evidence

The GDG used a number of criteria when deciding whether or not to accept unpublished data. First, the evidence must have been accompanied by a trial report containing sufficient detail to properly assess the quality of the data. Second, the evidence must have been submitted with the understanding that data from the study and a summary of the study's characteristics would be published in the full guideline. Therefore, the GDG did not accept evidence submitted as commercial in confidence. However, the GDG recognised that unpublished evidence submitted by investigators might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.

3.2.10 Data extraction

Study characteristics and outcome data were extracted from all eligible studies, which met the minimum quality criteria, using a Word-based form (see Appendix 16).

In most circumstances, for a given outcome (continuous and dichotomous), where more than 50% of the number randomised to any group were lost to follow up, the data were excluded from the analysis (except for the outcome 'leaving the study early', in which case, the denominator was the number randomised). Where possible, dichotomous efficacy outcomes were calculated on an intention-to-treat basis (that is, a 'once-randomised-always-analyse' basis). Where there was good evidence that those participants who ceased to engage in the study were likely to have an unfavourable outcome, early withdrawals were included in both the numerator and denominator. Adverse effects were entered into Review Manager as reported by the study authors because it is usually not possible to determine whether early withdrawals had an unfavourable outcome. Where there was limited data for a

particular review, the 50% rule was not applied. In these circumstances the evidence was downgraded due to the risk of bias.

Where some of the studies failed to report standard deviations (for a continuous outcome), and where an estimate of the variance could not be computed from other reported data or obtained from the study author, the following approach was taken.[3]

When the number of studies with missing standard deviations was less than a third and when the total number of studies was at least 10, the pooled standard deviation was imputed (calculated from all the other studies in the same meta-analysis that used the same version of the outcome measure). In this case, the appropriateness of the imputation was made by comparing the standardised mean differences (SMDs) of those trials that had reported standard deviations against the hypothetical SMDs of the same trials based on the imputed standard deviations. If they converged, the meta-analytical results were considered to be reliable.

When the conditions above could not be met, standard deviations were taken from another related systematic review (if available). In this case, the results were considered to be less reliable.

The meta-analysis of survival data, such as time to any drinking episode, was based on log hazard ratios and standard errors. Since individual patient data were not available in included studies, hazard ratios and standard errors calculated from a Cox proportional hazard model were extracted. Where necessary, standard errors were calculated from confidence intervals or p-value according to standard formulae (see the Cochrane Reviewers' Handbook 4.2.2.). Data were summarised using the generic inverse variance method using Review Manager.

Consultation with another reviewer or members of the GDG was used to overcome difficulties with coding. Data from studies included in existing systematic reviews were extracted independently by one reviewer and cross-checked with the existing data set. Where possible, two independent reviewers extracted data from new studies. Where double data extraction was not possible, data extracted by one reviewer was checked by the second reviewer. Disagreements were resolved through discussion. Where consensus could not be reached, a third reviewer or GDG members resolved the disagreement. Masked assessment (that is, blind to the journal from which the article comes, the authors, the institution and the magnitude of the effect) was not used since it is unclear that doing so reduces bias (Jadad *et al*., 1996; Berlin, 2001).

3.2.11 Synthesising the evidence

Meta-analysis

Where possible, meta-analysis was used to synthesise the evidence using Review Manager. If necessary, reanalyses of the data or sub-analyses were used to answer review questions not addressed in the original studies or reviews.

Dichotomous outcomes were analysed as relative risks (RR) with the associated 95% CI (for an example, see Figure 1). A relative risk (also called a risk ratio) is the ratio of

[3] Based on the approach suggested by Furukawa et al. (2006).

the treatment event rate to the control event rate. An RR of 1 indicates no difference between treatment and control. In Figure 1, the overall RR of 0.73 indicates that the event rate (that is, non-remission rate) associated with intervention A is about three quarters of that with the control intervention or, in other words, the relative risk reduction is 27%.

The CI shows with 95% certainty the range within which the true treatment effect should lie and can be used to determine statistical significance. If the CI does not cross the 'line of no effect', the effect is statistically significant.

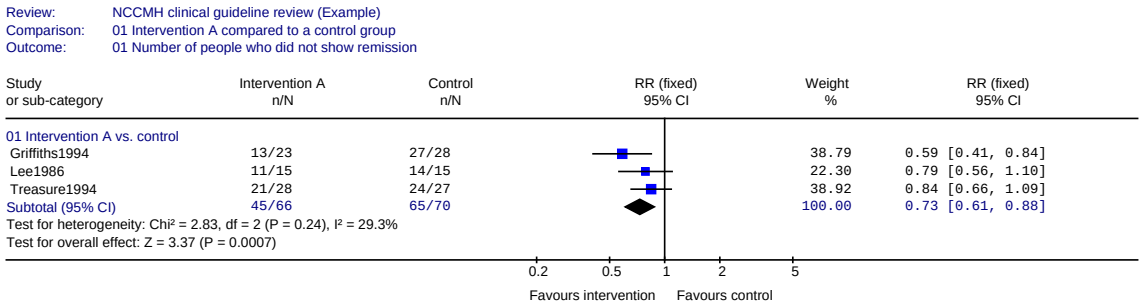


Figure 1: Example of a forest plot displaying dichotomous data

Continuous outcomes were analysed using the standardised mean difference (SMD) as different measures were used in different studies to estimate the same underlying effect (for an example, see Figure 2). If reported by study authors, intention-to-treat data, using a valid method for imputation of missing data, were preferred over data only from people who completed the study.

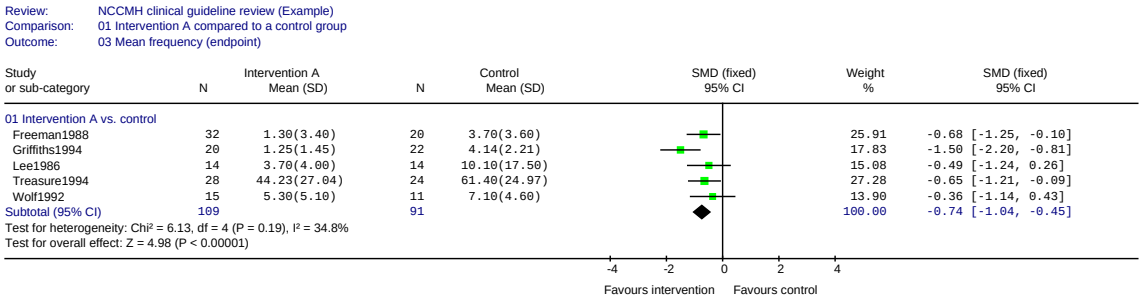


Figure 2: Example of a forest plot displaying continuous data

The Number Needed to Treat for Benefit (NNTB) or the Number Needed to Treat for Harm (NNTH) was reported for each outcome where the baseline risk (i.e. control group event rate) was similar across studies. In addition, NNTs calculated at follow-up were only reported where the length of follow-up was similar across studies. When the length of follow-up or baseline risk varies (especially with low risk), the NNT is a poor summary of the treatment effect (Deeks, 2002).

Heterogeneity

To check for consistency of effects among studies, both the I^2 statistic and the chi-squared test of heterogeneity, as well as a visual inspection of the forest plots were used. The I^2 statistic describes the proportion of total variation in study estimates that is due to heterogeneity (Higgins & Thompson, 2002). The I^2 statistic was interpreted in the follow way based on Higgins and Green (2009):

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity.

Two factors were used to make a judgement about importance of the observed value of I^2: a) the magnitude and direction of effects, and b) the strength of evidence for heterogeneity (for example, P value from the chi-squared test, or a confidence interval for I^2).

Publication bias

To explore the possibility that the results entered into each meta-analysis suffered from publication bias, data from included studies were entered, where there was sufficient data, into a funnel plot. Asymmetry of the plot was taken to indicate possible publication bias and investigated further.

Where necessary, an estimate of the proportion of eligible data that were missing (because some studies did not include all relevant outcomes) was calculated for each analysis.

3.2.12 Presenting the data to the GDG

Study characteristics tables and, where appropriate, forest plots generated with Review Manager were presented to the GDG.

Where meta-analysis was not appropriate and/or possible, the reported results from each primary-level study were included in the study characteristics table (and where appropriate, in a narrative review).

Evidence profile tables

A GRADE[4] evidence profile was used to summarise both the quality of the evidence and the results of the evidence synthesis (see Table 3 for an example of an evidence profile). The GRADE approach is based on a sequential assessment of the quality of evidence, followed by judgment about the balance between desirable and undesirable effects, and subsequent decision about the strength of a recommendation.

For each outcome, quality may be reduced depending on the following factors:

- **study design** (randomised trial, observational study, or any other evidence)
- **limitations** (based on the quality of individual studies)
- **inconsistency** (see section 1.5.4 for how consistency was assessed)
- **indirectness** (that is, how closely the outcome measures, interventions and participants match those of interest)
- **imprecision** (based on the confidence interval around the effect size).

For observational studies, the quality may be increased if there is a large effect, plausible confounding would have changed the effect, or there is evidence of a dose-response gradient (details would be provided under the other considerations

[4] For further information about GRADE, see www.gradeworkinggroup.org

column). Each evidence profile also included a summary of the findings: number of patients included in each group, an estimate of the magnitude of the effect, and the overall quality of the evidence for each outcome.

Table 4: Example of GRADE evidence profile

Quality assessment							Summary of findings				
							No. of patients		Effect		Quality
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative (95% CI)	Absolute	
Outcome 1											
6	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1,2]	none	8/191	7/150	RR 0.94 (0.39 to 2.23)	0 fewer per 100 (from 3 fewer to 6 more)	□□□□ LOW
Outcome 2											
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	120/600	220/450	RR 0.39 (0.23 to 0.65)	30 fewer per 100 (from 17 fewer to 38 fewer)	□□□□ HIGH
Outcome 3											
3	randomised trials	no serious limitations	serious inconsistency[3]	no serious indirectness	very serious[1,2]	none	83	81	-	MD -1.51 (-3.81 to 0.8)	□□□□ VERY LOW
Outcome 4											
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	88	93	-	SMD -0.26 (-0.50 to -0.03)	□□□□ MODERATE
Outcome 5											
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1,2]	none	109	114	-	SMD -0.13 (-0.6 to 0.34)	□□□□ LOW

[1] Optimal information size not met.
[2] The CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.
[3] Considerable heterogeneity.

3.2.13 Forming the clinical summaries and recommendations

Once the GRADE evidence profiles relating to a particular review question were completed, summary evidence tables were developed (these tables are presented in the evidence chapters). Finally, the systematic reviewer in conjunction with the topic group lead produced a clinical evidence summary.

Once the GRADE profiles and clinical summaries were finalised and agreed by the GDG, the associated recommendations were drafted. In making recommendations, the GDG took into account the trade-off between the benefits and downsides of treatment as well as other important factors, such as economic considerations, values of the development group and society, and the group's awareness of practical issues (Eccles *et al.*, 1998).

3.2.14 Method used to answer a review question in the absence of appropriately designed, high-quality research

In the absence of appropriately designed, high-quality research, or where the GDG were of the opinion (on the basis of previous searches or their knowledge of the literature) that there were unlikely to be such evidence, an informal consensus process was adopted. This process focused on those questions that the GDG considered a priority.

Informal consensus

The starting point for the process of informal consensus was that a member of the topic group identified, with help from the systematic reviewer, a narrative review that most directly addressed the review question. Where this was not possible, a brief review of the recent literature was initiated.

This existing narrative review or new review was used as a basis for beginning an iterative process to identify lower levels of evidence relevant to the review question and to lead to written statements for the guideline. The process involved a number of steps:

1. A description of what is known about the issues concerning the clinical question was written by one of the topic group members.
2. Evidence from the existing review or new review was then presented in narrative form to the GDG and further comments were sought about the evidence and its perceived relevance to the review question.
3. Based on the feedback from the GDG, additional information was sought and added to the information collected. This may include studies that did not directly address the review question but were thought to contain relevant data.
4. If, during the course of preparing the report, a significant body of primary-level studies (of appropriate design to answer the question) were identified, a full systematic review was done.
5. At this time, subject possibly to further reviews of the evidence, a series of statements that directly addressed the review question were developed.

6. Following this, on occasions and as deemed appropriate by the development group, the report was then sent to appointed experts outside of the GDG for peer review and comment. The information from this process was then fed back to the GDG for further discussion of the statements.
7. Recommendations were then developed and could also be sent for further external peer review [amend as appropriate].
8. After this final stage of comment, the statements and recommendations were again reviewed and agreed upon by the GDG.

3.2.15 Health economics methods

The aim of the health economics was to contribute to the guideline's development by providing evidence on the cost effectiveness of interventions for alcohol misuse covered in the guideline. This was achieved by:

- systematic literature review of existing economic evidence
- decision-analytic economic modelling.

Systematic reviews of economic literature were conducted in all areas covered in the guideline. Economic modelling was undertaken in areas with likely major resource implications, where the current extent of uncertainty over cost effectiveness was significant and economic analysis was expected to reduce this uncertainty, in accordance with the *Guidelines Manual* (NICE, 2009). Prioritisation of areas for economic modelling was a joint decision between the Health Economist and the GDG. The rationale for prioritising review questions for economic modelling was set out in an economic plan agreed between NICE, the GDG, the Health Economist and the other members of the technical team. The following economic questions were selected as key issues that were addressed by economic modelling:

1) What is the preferred method of medically-assisted withdrawl, in terms of clinical and cost-effectiveness (taking into consideration the benefits/adverse effects) and for which people and in which setting (taking into account the nature of intervention in each setting)?
   - Community (taking into account levels of supervision: structured vs. unstructured day programme)
   - Residential
   - Inpatient: Mental health or acute hospital
   - Prisons

2) For people with alcohol dependence or harmful alcohol use, which pharmacological interventions aimed at attenuation of driniking/maintenance of abstinence are clinically and cost-effective?

3) For people with alcohol dependence or harmful alcohol use, which psychological and psychosocial interventions aimed at attenuation of drinking/maintenance of abstinence are clinically and cost-effective?

4) For people with alcohol dependence or harmful alcohol use, which combination of psychological/psychosocial and pharmacological interventions aimed at attenuation of drinking/maintenance of abstinence are clinically and cost-effective?

In addition, literature on the health-related quality of life of people with alcohol-use disorders was systematically searched to identify studies reporting appropriate utility scores that could be utilised in a cost-utility analysis.

The rest of this section describes the methods adopted in the systematic literature review of economic studies. Methods employed in economic modelling are described in the respective sections of the guideline.

3.2.16 Literature search strategy for economic evidence

Scoping searches

A broad preliminary search of the literature was undertaken in September 2008 to obtain an overview of the issues likely to be covered by the scope, and help define key areas. Searches were restricted to economic studies and health technology assessment reports, and conducted in the following databases:

- EMBASE
- MEDLINE / MEDLINE In-Process
- Health Technology Assessment (HTA) database (technology assessments)
- NHS Economic Evaluation Database (NHS EED)

Systematic literature searches

After the scope was finalised, a systematic search strategy was developed to locate all the relevant evidence. The balance between sensitivity (the power to identify all studies on a particular topic) and specificity (the ability to exclude irrelevant studies from the results) was carefully considered, and a decision made to utilise a broad approach to searching to maximise retrieval of evidence to all parts of the guideline. Searches were restricted to economic studies and health technology assessment reports, and conducted in the following databases:

- CINAHL
- EconLit
- EMBASE
- MEDLINE / MEDLINE In-Process
- PsycINFO
- Health Technology Assessment (HTA) database (technology assessments)
- NHS Economic Evaluation Database (NHS EED)

* Any relevant economic evidence arising from the clinical scoping searches was also made available to the health economist during the same period.

For standard mainstream bibliographic databases (CINAHL, EMBASE, MEDLINE and PsycINFO) search terms on alcohol dependence and harmful alcohol use were combined with a search filter for health economic studies. For searches generated in topic-specific databases (HTA, NHS EED) search terms on alcohol dependence and harmful alcohol use were used without a filter. The sensitivity of this approach was aimed at minimising the risk of overlooking relevant publications, due to inaccurate or incomplete indexing of records on

the databases, as well as potential weaknesses resulting from more focused search strategies (e.g. for interventions).

Reference Manager
Citations from each search were downloaded into Reference Manager (a software product for managing references and formatting bibliographies) and duplicates removed. Records were then screened against the inclusion criteria of the reviews before being quality appraised. To keep the process both replicable and transparent, the unfiltered search results were saved and retained for future potential re-analysis.

Search filters
The search filter for health economics is an adaptation of a filter designed by Centre for Reviews and Dissemination (CRD). The filter comprises a combination of controlled vocabulary and free-text retrieval methods.

Date and language restrictions
Systematic database searches were initially conducted in June 2008 up to the most recent searchable date. Search updates were generated on a 6-monthly basis, with the final re-runs carried out in March 2010 ahead of the guideline consultation. After this point, studies were included only if they were judged by the GDG to be exceptional (for example, the evidence was likely to change a recommendation).

Although no language restrictions were applied at the searching stage, foreign language papers were not requested or reviewed, unless they were of particular importance to an area under review. All the searches were restricted to research published from 1993 onwards.

Other search methods
Other search methods involved scanning the reference lists of all eligible publications (systematic reviews, stakeholder evidence and included studies from the economic and clinical reviews) to identify further studies for consideration.

Full details of the search strategies and filter used for the systematic review of health economic evidence are provided in Appendix 12.

3.2.17 Inclusion criteria for economic studies

The following methods were applied to select studies identified by the economic searches for further consideration.

No restriction was placed on language or publication status of the papers.
Studies published from 1998 onwards that reported data from financial year 1997/98 onwards were included. This date restriction was imposed in order to obtain data relevant to current healthcare settings and costs.
Only studies from Organisation for Economic Co-operation and Development countries were included, as the aim of the review was to identify economic information transferable to the UK context.

Selection criteria based on types of clinical conditions and patients as well as interventions assessed were identical to the clinical literature review.

Studies were included provided that sufficient details regarding methods and results were available to enable the methodological quality of the study to be assessed, and provided that the study's data and results were extractable. Poster presentations of abstracts were excluded; however, they were included if they reported utility data required for a cost-utility analysis, when no other data were available.

Full economic evaluations that compared two or more relevant options and considered both costs and consequences (that is, cost–consequence analysis, cost effectiveness analysis, cost–utility analysis or cost–benefit analysis) as well as cost- analyses that compared only costs between two or more interventions were included in the review.

Economic studies were included if they used clinical effectiveness data from an RCT, a prospective cohort study, or a systematic review and meta-analysis of clinical studies. Studies that had a mirror-image or other retrospective design were excluded from the review.

Studies were included only if the examined interventions were clearly described. This involved the dosage and route of administration and the duration of treatment in the case of pharmacological therapies; and the types of health professionals involved as well as the frequency and duration of treatment in the case of psychological interventions. Evaluations in which medications were treated as a class were excluded from further consideration.
Studies that adopted a very narrow perspective, ignoring major categories of costs to the NHS, were excluded; for example studies that estimated exclusively drug acquisition costs or hospitalisation costs were considered non-informative to the guideline development process.

3.2.18 Applicability and quality criteria for economic studies

All economic papers eligible for inclusion were appraised for their applicability and quality using the methodology checklist for economic evaluations recommended by NICE (NICE, 2009), which is shown in Appendix 13 of this guideline. The methodology checklist for economic evaluations was also applied to the economic models developed specifically for this guideline. All studies that fully or partially met the applicability and quality criteria described in the methodology checklist were considered during the guideline development process, along with the results of the economic modelling conducted specifically for this guideline.

3.2.19 Presentation of economic evidence

The economic evidence considered in the guideline is provided in the respective evidence chapters, following presentation of the relevant clinical evidence. The references to included studies and to those potentially relevant that did not meet the inclusion criteria can be found in Appendix 19, as well as the evidence tables with the characteristics and results of economic studies included in the review. Methods and results of economic modelling undertaken alongside the guideline development process are presented in the relevant evidence chapters. Characteristics and results of all economic studies considered during the guideline development process (including

modelling studies conducted for this guideline) are summarised in economic evidence profiles accompanying respective GRADE clinical evidence profiles in Appendix 18.

3.2.20 Results of the systematic search of economic literature

Publications that were clearly not relevant to the topic (i.e. economic issues and information on health-related quality of life in people with alcohol misuse) were excluded at the sifting stage first. The abstracts of all potentially relevant publications were then assessed against the inclusion criteria for economic evaluations by the health economist. Full texts of the studies potentially meeting the inclusion criteria (including those for which eligibility was not clear from the abstract) were obtained. Studies that did not meet the inclusion criteria, were duplicates, were secondary publications of one study, or had been updated in more recent publications were subsequently excluded. Economic evaluations eligible for inclusion were then appraised for their applicability and quality using the methodology checklist for economic evaluations. Finally, economic studies that fully or partially met the applicability and quality criteria were considered at formulation of the guideline recommendations.

3.2.21 Stakeholder contributions

Professionals, service users, and companies have contributed to and commented on the guideline at key stages in its development. Stakeholders for this guideline include:

- service user/carer stakeholders: the national service user and carer organisations that represent people whose care is described in this guideline
- professional stakeholders: the national organisations that represent health care professionals who are providing services to service users
- commercial stakeholders: the companies that manufacture medicines used in the treatment of alcohol dependence and harmful alcohol use
- Primary Care Trusts
- Department of Health and Welsh Assembly Government.

Stakeholders have been involved in the guideline's development at the following points:

- commenting on the initial scope of the guideline and attending a briefing meeting held by NICE
- contributing possible review questions and lists of evidence to the GDG
- commenting on the draft of the guideline
- highlighting factual errors in the pre-publication check.

3.2.22 Validation of the guideline

Registered stakeholders had an opportunity to comment on the draft guideline, which was posted on the NICE website during the consultation period. Following the consultation, all comments from stakeholders and others were responded to, and the guideline updated as appropriate. The GRP also reviewed the guideline and checked that stakeholders' comments had been addressed.

Following the consultation period, the GDG finalised the recommendations and the NCCMH produced the final documents. These were then submitted to NICE for the pre-publication check where stakeholders are given the opportunity to highlight

1 factual errors. Any errors are corrected by the NCCMH, then the guideline is formally
2 approved by NICE and issued as guidance to the NHS in England and Wales.
3

4

4. Experience of care

4.1 Introduction

This chapter provides an overview of the experience of people with alcohol problems, and their families/carers. The first section comprises first-hand personal accounts written by people who have experienced alcohol problems and carers, which provide an understanding of alcohol dependence and harmful alcohol use, accessing services, having treatment and caring for someone with an alcohol problem. It should be noted that these accounts are not representative of the experiences of people with alcohol problems and therefore can only ever be illustrative. The second section of the chapter includes a review of the qualitative literature and a thematic analysis of accounts from children with parents who misuse alcohol, which provide a basis for the recommendations, found at the end of the final section.

4.2 Personal accounts—alcohol dependence and harmful alcohol use

4.2.1 Introduction

The writers of the personal accounts from people with alcohol problems were contacted through representatives on the GDG and through various agencies that had access to people with alcohol problems. The people who were approached to write the accounts were asked to consider a number of questions when composing their narratives. These included:

- When did you first seek help for your alcohol problem and whom did you contact? (Please describe this first contact.)
- What helped or did not help you gain access to services? Did a friend or family member help you gain access to these services?
- Do you think that any life experiences led to the onset of the problem? If so, please describe if you feel able to do so.
- In what ways has the alcohol problem affected your everyday life (such as education, employment and making relationships) and the lives of those close to you?
- What possible treatments were discussed with you?
- What treatment(s) did you receive? Please describe any drug treatment and/or psychological therapy.
- Was the treatment(s) helpful? (Please describe what worked for you and what didn't work for you.)
- How would you describe your relationship with your practitioner(s) (for example, your GP, alcohol service worker or other)
- Did you use any other approaches to help your alcohol problem in addition to those provided by NHS services, for example private treatment? If so please describe what was helpful and not helpful.
- Do you have any language support needs, including needing help with reading or speaking English? If so, did this have an impact on your understanding of the alcohol problem or on receiving treatment?

- Did you attend a support group and was this helpful? Did family and friends close to you or people in your community help and support you?
- How has the nature of the problem changed over time?
- How do you feel now?
- If your alcohol problem has improved, do you use any strategies to help you to stay well? If so, please describe these strategies.

Each author signed a consent form allowing the account to be reproduced in this guideline. Three personal accounts from people with alcohol problems (one woman and two men) were received in total. All of the people who provided an account had experienced long-standing (almost life-long) problems with alcohol and identified themselves as 'alcoholic'. All said that they had difficulty in admitting to themselves that there was a problem, and two also had depression. Most reported that their drinking had had a serious impact on their lives, with family, employment and health being the commonly affected areas. Two of the people engaged in criminal behaviour while dependent on alcohol.. All of the people who wrote accounts had accessed treatment after many years of drinking; while they sought help from different services (primary care, secondary mental health services and alcohol services) all entered detoxification programmes (one of which was prison based). Experiences of detoxification programmes were mixed: one person who had been in programmes in a psychiatric hospital and in prison, preferred the prison programme. Two people initially found the programme helpful but they relapsed shortly after. Two people found rehabilitation programmes helpful; one person relapsed following treatment but the other person found the programme to be foundation on which his sobriety was built (as well as attending Alcoholics Anonymous). One person found that the combination of an alcohol treatment programme and a detoxification programme provided the base on which to build a new life. Two people had attended Alcoholics Anonymous and experiences were mixed. One person had private treatment with naltrexone, which had not been helpful.

4.2.2 Personal account A

It was in 2001: I was 48 years old and standing outside a shopping centre when a fellow alcoholic walked towards me. I said 'hello' and he just stabbed me in the stomach. I was taken to hospital and treated as an inpatient for 10 days. In the morning I woke up with the DTs. A nurse came by and said I was suffering from shock and I answered that it was the DTs and that I was an alcoholic.

I took my first drink in a pub at 14 years old; I then had a successful 25-year career with a brewery and was always a heavy drinker. The drinking became a serious problem when my career and marriage ended in 1993, by which time, in hindsight, I would say I was an alcoholic.

In hospital doctors began to treat me for alcohol dependency, which consisted only of medication (daily doses of Librium), and on my release from hospital referred me to an alcohol treatment centre for assessment to decide which type/level of treatment I needed. It was the first time I had ever admitted that I had a problem, even to myself.

When I was released from hospital I returned to my YMCA hostel and resumed where I left off—drinking cider 24/7 in my room, breaking the rules at the hostel. While in

the streets with my 'friends', I totally disregarded my referral to the treatment centre and went on my merry way towards oblivion.

When I returned to the hostel the staff were constantly on my case to get help. I was searched on my way in and my room was searched on an ad hoc basis to ensure I wasn't drinking or taking drugs (a minor pastime I had developed) on the premises. I began to feel persecuted and quite bitter, and I showed my anger at my hostel key working sessions. However, when I was sober enough, which was very rare, I did admit to needing help.

So in January 2002 I went to the alcohol treatment centre and was assessed. They informed me I would need medical detoxification and they would help to get a place; I was offered weekly key working sessions and advice in the meantime.

I had to wait 10 months to get a detox placement at a psychiatric hospital. During that time I had to go to my weekly sessions, which I nearly gave up on quite a few times but the hostel staff kept on encouraging me to go, no matter how drunk I was, until I took up my placement.

Detox was really hard for me despite the medication— I was disorientated, nauseous, shaking all the time, and I heard things almost constantly; I also couldn't hold a knife and fork so I could not eat hot food. On top of this, I had to attend two group sessions a day in the morning and evening, plus daily key working sessions, and have a daily injection of vitamin B plus my medication four times a day. However, after 2 weeks, even though I was still quite shaky, I was at last functioning and through the group sessions I began to realise what I had been doing to my body and my mind.

Towards the end of my time in the detox ward I contacted my keyworker at the YMCA hostel with a view to returning but after discussion we decided, as I was not in receipt of funding and had no care/social worker to help with any further support to recover, that I would attend an alcohol rehabilitation centre run by the YMCA for 6 months. This enabled me to have continuous YMCA residency, which also meant I would be able to return to the hostel after the 6 months.

The rehabilitation centre was really good for me; the staff were professional, tolerant and understanding. I learnt that my style of recovery there was eclectic and made up of the centre's own ideas plus bits of 12 step, CBT and holistic therapies plus transactional analysis. Group sessions took place daily in the morning followed by a staff and group lunch cooked by residents nominated for that day; cleaning and gardening were also chores for the residents so that we could learn our life skills again. We also went shopping so we could learn how to budget (that is, live within our means and not rely on shoplifting or some other kind of theft or fraud). The group sessions were varied, covering relapse prevention, life stories, self-esteem, self-confidence and triggers. Other topics, which were linked to recovery, were art therapy and open groups were we could talk about anything that affected us. I seemed to do OK and after 6 months I returned to the YMCA hostel a sober man for the first time in 15 years.

I did not think I needed anymore support or treatment. I felt really fit both physically and mentally, and so resumed my previous friendships/relationships within the hostel feeling I was strong enough to stay clear of alcohol and drugs, but I was wrong.

In hindsight I think I planned my relapse. I left the rehab centre on a Monday and took my first drink (a can of cider), 4 days later on the Friday with the other drinkers at a park bench thinking I could leave it at that, but by the end of the day I was totally drunk. I woke up next morning with a 3 litre bottle at the side of the bed and instinctively reached down for the first drink of the day, and, as soon as that was gone and feeling quite ill, I made my way to the off-licence and was back to square one. The relapse hit me very hard. All I could do was hide away from any family who would talk to me (only one son) and everyone who had supported my recovery. My denial was total and as I got worse so did the shoplifting and begging.

It was whilst I was trying to outrun two security guards after stealing a three litre bottle of cider and a bottle of vodka that I had my first heart attack. I was taken to hospital and treated, but as soon as I was well enough the police arrested me for theft. Two days later I had a mild stroke and was strongly advised by my consultant to go back into recovery, but on my release I reasoned it hadn't worked the first time so why should it now? So I just traded on whatever sympathy I could get and just carried on as before.

A couple of months later I got into a drunken brawl followed by an altercation with the officers who were breaking it up and I suffered a more serious heart attack and again I ended up in hospital. But by now the doctors, police and the hostel were completely fed up with my antisocial behaviour as were the supermarkets, off-licences and just about everyone else. On my recovery I was arrested and in court I was given an ultimatum—either take treatment willingly myself or go to prison, which I did not want. So I again entered treatment, which the police insisted on as they were adamant I would return to my old behaviour.

My start in treatment was the same as the first time but much quicker—it began within 5 weeks at the alcohol treatment centre plus detox at the psychiatric hospital. This time I got funding for my rehabilitation which was at a different centre, but which offered a very similar style of treatment to where I was first treated. After 6 months I was offered the chance to extend my recovery period by entering a third-stage supported house, which was a semi-independent unit. I decided I needed this.

I had another stroke whilst at the supported house. After 14 months as a resident, and with the help and support of the staff of the rehabilitation centre, I got my own flat and have remained alcohol and drug free for the last 6 years. My physical health is still giving my consultants cause for concern but I am recovering slowly and as soon as I am fit enough to undergo surgery I am hoping one day to be fit enough to return to the workplace. However, my years of abuse have cost me a high price in terms of my career, home, marriage, family (four children whom I didn't see for 10 years) and my health.

I have to say I could not have achieved any of this without all the support I have received from the YMCA (the hostel and rehabilitation centre), the hospitals, the

alcohol treatment centre, the rehabilitation centre who ran the supported house where I was a resident and, begrudgingly, the police who were really very good about things considering my atrocious antisocial behaviour.

I have worked hard to restore my relationships with my four children and two grandchildren, and have had considerable success. I had support throughout this process from my keyworker, to whom I will be forever grateful, and my ex-wife who I always thought, through my drunken years, hated my guts (she didn't – she just wanted me to get back to living again).

Now I feel fairly good about myself and what I have achieved. But I don't feel pride in myself and I will never forgive myself for the man I became nor for the hurt I have caused the people I love and the things I have done. Also I am afraid to get too close to people or commit to any relationship because I feel I can never completely trust myself again. But, having said that and having explained the reasons to my current girlfriend, who is understanding of my fears, I am making positive headway in 'trusting me'.

4.2.3 Personal account B

I am 55 and I started drinking heavily 2 years ago. I had been drinking for a long time before that and was dependent on alcohol, but I thought I was in control. For a while I went to work and no one noticed there was a problem. Alcoholics always say they can handle it and that is also what I thought. But then it did start to affect my ability to do my job and one day I lost it and drove a car into the building where I worked. So I lost my job and my licence, and my stepmother had also recently died and so I started drinking heavily after this. I was always being picked up by the police and I also tried to commit suicide at this point in my life.

When I was not drinking so much I tried to get help because my family wanted me to. I went to my GP first of all as he had always been helpful. He recommended I go to my local drug and alcohol service, and they sent me to a residential mental health hospital where I went on their detoxification programme on a voluntary basis. It was not a nice place at all, and the workers seemed far more concerned in getting people clean of heroin rather than helping people with alcohol problems. I was only there for 2 weeks and it did not help much. I went back to drinking when I got out.

But over the next few years I had to go back to that ward twice for a week at a time because of my mental health problems (I had acute depression and had attempted suicide) and I also had another detoxification. I hated the attitude of the staff--I was supposed to have a meeting with the special care workers three times a week but it never happened. The groups were mostly made up of young people and they were drinkers and drug users together, so this did not work for me. The door was always locked and I felt I was a prisoner. The people I met all went back to booze. They wanted me to go to a rehabilitation place in the country, but I wouldn't go because it was for a year and it meant I would not see my family.

When I was made to go to another hospital I saw a real difference in attitudes. The door was always open and one of the workers chatted to me for over an hour. I was only there for one night but if it had been longer I think it would have helped far more than the other hospital. They were there to help drinkers as much as drug users.

My family was there for me when I was drinking. They told me early on that I had a drink problem but I always denied it. I was stealing from them and one weekend I even stole my son's whisky, which he was keeping for a special occasion. I denied it but then I realised what was happening to me and tried to get help. I live with my Mum in her house with my son and I have two brothers with families and a sister in Australia. They always tried to get me to get help. My Dad was there for me too.

It was only earlier this year I realised I had a real problem and I needed help so I went back to hospital but I was barred because the last time I turned up and said I wanted help I was drunk. Their policy is that you can't turn up intoxicated.

I hit rock bottom when I was arrested for common assault in August 2009 and was sent to prison the next month. I went into detox on one of the wards. The staff were very good--they should swap jobs with staff in other services so other workers can see how it should be done when helping drinkers. I was always checked on, and I was able to talk to the officers and the therapists. I spent 2 weeks on this ward, and 2 weeks on another ward. Someone from Adfam came and saw me and kept in touch after I left. It helped to have someone in touch with the family and me. She is non-judgemental and says I can phone her when I need to talk.

I had a 3-month sentence but I only did a month because of good behaviour. I had no idea I was going out. They woke me up at 6.30 and said 'off you go' so I phoned my Mum. I was really shocked and at the beginning thought it was a joke. But going home clean made me and the family really happy.

I started going to AA and liked it because it was for alcoholics who were more my age. But it was on Saturdays which made it difficult to attend so I have not been recently.

I have cravings and triggers but I can control them. I think of something else and do something else like make myself a cup of tea. I still have good support from my GP who is a real family doctor and looks after my Mum. I really trust him. I am determined not to drink again.

When I was a drinker I hated the way people treated me. They judge you without knowing you because of what you look like as a drinker. I think it is harder to get off drink than drugs. It can kill you getting off alcohol and people do not know this--they think you can just stop. People seem to have more sympathy with drug addicts rather than alcoholics. People need to be educated about this, they just don't understand.

I think services should get people who have managed to stop drinking to talk to others to help them. Experience is really important.

4.2.4 Personal account C

From a very early age my lifestyle was somewhat alcohol-orientated in as much as I started work at 16 in the shipping industry where alcohol was available on board ship at any time of day or night. We seemed to accept that this was part of our working life, although I never felt at that time as if I was dependent upon drinking alcohol. Outside

of work my sporting interests also involved much alcohol. It is clear to me now that alcoholism is a progressive illness and it was later in life that my dependency was determined.

My problem in the early stages did not seem to have affected my education or professional life. Indeed I went on to be very successful in my profession. However I realise that latterly I was a 'working alcoholic'. It was at this time and as I retired that the lives of my wife and close family were badly affected. Although they initially supported me in seeking help I was not ready and really only paid 'lip service' to the help available just to please them. I really had no thought about how I was tearing the lives of my family apart.

I denied any alcohol problem although I was told by my GP to stop drinking. However, my GP seemed to distance himself from the alcohol problem. In September 2001 I was diagnosed with severe depression and prescribed antidepressants. My GP also referred me to an antidepressant clinic, where I received individual counselling together with group therapy. I attended the clinic for a number of years—but I still drank.

At one stage I tried private treatment which consisted of a one-to-one consultation and a prescription of naltrexone which I was to take when I felt the desire to drink or was subjected to an alcoholic environment. This was supposed to reduce my urge to drink at that time. However this did not help me at all although the clinic claims a huge success rate.

In early 2005, even after attending the antidepressant clinics and seeking private treatment for heavy drinking, I was in a desperate state and contacted the Alcoholics Anonymous helpline. I attended AA meetings all that year.

On one occasion, while very much under the influence of drink, I was taken by my wife and daughter to the GP's surgery and saw the practice nurse who immediately referred me to the local psychiatric hospital where I stayed for about a week for detoxification before being discharged. I then attended an alcohol/drug centre which led to an interview with a local alcohol and drug agency. The agency gave me one-to-one counselling before I was introduced to the 12 step programme, which had strict rules of no alcohol intake and attendance at at least three AA meetings per week. After 3 weeks into the course, I was banned from attending AA meetings because I was under the influence of drink. I was also suspended from the agency.

I was nearly 70 years of age before I finally agreed to attend an interview at a rehabilitation centre. After then refusing to go to the first interview, with the encouragement of counsellors from the agency I entered a rehabilitation centre for primary rehabilitation. I was in primary rehabilitation for 6 weeks and completed steps one to five. I opted to continue into secondary rehabilitation for 12 weeks, completing steps six to twelve. I was given an intensive course of treatment consisting of one-to-one counselling and an in-depth understanding of the 12 step programme.

The treatment at the centre, and afterwards supported by the agency and AA, was incredible. The 12 step programme with the agency did not work for me as it was only

one day per week and I did not have any self-control over my drinking for the other 6 days, whereas the intensive course in rehab gave me the concentration of mind I needed away from outside influences.

I still attend AA meetings which are an essential part in keeping me in sobriety and are helpful not just for me but others in recovery. The fact that it is anonymous enables us to talk frankly and open without fear. My family, especially my wife who attends Al-Anon meetings, are very supportive. In the first 6 months of recovery I also attended aftercare sessions at the rehabilitation centre. Friends and community groups were also very supportive. Close friends and relations helped me considerably during the times when I was completely under the influence of alcohol, taking me to hospital, sitting and talking to me and generally supporting my wife and family. The community groups I belonged to supported me the best way they could and by not rejecting me. In recovery both friends and the community groups have supported me and welcomed me without reservation. Because of my heavy drinking I was not really aware of the support I received in those early days and it was some time before I really appreciated it.

The nature of my problem has changed in as much as I am still an alcoholic but I do not drink. Life now is 'beyond my dreams'—there has been such an incredible change in my life and the lives of my family. However, I am still an alcoholic and live with the fear of going back to those dreadful days. I also live with guilt, anger and resentfulness of the things that have happened and for what I inflicted on others during my years of drinking. I have to learn to control these feelings. It all takes time, as does the trust I have to regain from all whom I hurt and cheated. When it does come, and it comes slowly, it is the greatest gift. I am lucky that after years of abusing my body physically and mentally, now at the age of nearly 75 I am fit and well.

We all have our own ways of handling our lives in sobriety. However most of us acknowledge that talking to fellow alcoholics and close family is the best strategy for continuing in recovery. If we do not—and it does happen when we get into a 'comfort zone'—then it shows in the way we conduct ourselves. Even now after 4 years of sobriety I fail in this area, which causes problems with my close family, especially my wife. The one basic rule is not to take the first drink, day by day.

4.3 Personal accounts—carers

4.3.1 Introduction

The methods used for obtaining the carers' accounts were the same as outlined in section 1.2.1 but the questions included:

- In what way do you care for someone with an alcohol problem?
- How long have you been a carer of someone with an alcohol problem?
- In what ways has being a carer affected your everyday life (such as schooling, employment and making relationships) and the lives of those close to you?
- How involved are/were you in the treatment plans of the person with an alcohol problem?

- Were you offered support by the person's practitioners (for example, their GP, alcohol service worker, or other)?
- How would you describe your relationship with the person's practitioner(s)?
- Have you and your family been offered help or received assessment/treatment by a healthcare professional?
- Did you attend a support group and was this helpful?
- Did any people close to you help and support you in your role as a carer?

Although only two personal accounts from carers of people with alcohol problems were received, there is some consistency in the issues and concerns raised. First, there is a reluctance to use the word 'carer' in this context, which is an issue that is often raised by family and friends who are involved with people with problems with alcohol and drugs. Lack of support and communication from healthcare professionals and other staff, and issues around confidentiality, together with the stress and emotional impact on the family, are raised in both accounts. The families had tried for years to get the right help and their involvement with mental health services, alcohol services and the police had been problematic. While both accounts indicate that life with someone who has an alcohol problem can be very unsettled, both carers had found support for themselves, which had helped put things into perspective, and they brought coping skills to their role as supportive family member.

4.3.2 Carer account A

I remember very clearly the first time I felt I had become a carer of my youngest son, who was 16 at the time. It was around 9pm one evening 13 years ago. This night would surely stay in my memory for ever. A young person who was completely out of control arrived home and brought mayhem to the family. He produced a large knife and I was standing at the other end of it in my kitchen not knowing what to do. Watching four policemen restrain my son and take him away shouting and screaming left us feeling numb with disbelief. This was the first time my son had got drunk and the 13 years since that first night have been a rollercoaster and have changed the lives of the whole family. It was when I seemed to begin to 'care for' instead of 'care about' my son. Over those years huge changes have taken place in my life and the lives of my husband and my older son. Many people in the local community have also been affected, and the devastation has been vast. I never saw myself as a carer, however my life took on a completely different meaning.

Living with someone with an alcohol addiction does not stop life going on in other areas. During this time, my Dad had a heart attack and died in front of me. My Mum got sick and I was told she was going to die. I moved in with her for the last 5 weeks of her life to care for her while my husband tried to cope at home. Each morning I would hear stories from my husband involving the police, ambulance service and so on, and of the horror of the evening before. This is just one example of how life does not stop because you have someone misusing alcohol. It became a huge balancing act.

My physical health suffered—I developed chronic fatigue syndrome and I went into a severe depression where I just felt I could not deal with life any longer. I remember clearly how close I came to taking my own life, but it really did seem to be the only way to escape the horrendous knock-on effect of watching my son getting sicker and sicker and slowly destroying his life. I had to give up work which led to financial

implications and more stress for my husband. My relationship with my husband was affected hugely, and my relationship with my older son was also suffering. Any social life stopped when we became too afraid to leave the house, and holidays became non-existent. My whole day seemed to be geared towards trying to provide emotional and practical help to someone who just seemed to be going deeper and deeper into despair. I remember the evening we went out for 2 hours and came home to my son collapsed over the gas hob with two rings on and his arm inches away from the flame. Ten more minutes I am not sure we would have had a house to come home to or a son.

Over time we experienced violence towards ourselves, had many things smashed in the house, sat in police waiting rooms and court rooms, and found our son with both arms slashed by a razor. On one occasion we went from visiting our eldest son at university, to going straight to a young offenders institute to see our youngest son. Being completely naive about prison we felt humiliated and ashamed and tried to hold back the tears when our young lad appeared with a swollen face and black eye. I spent the 70-mile journey home sobbing my heart out.

I sat by his bedside whilst he was on a drip after trying to take his own life for the second time; on the third occasion he insisted we did not call for help—we had to wait for him to be unconscious before doing so. Imagine how that felt when you knew it would be so easy to do nothing and hope that all the pain would stop, for him and for us. Only people who have been in this situation would know how we could even begin to think like this! It's so hard to believe it yourself, but the continuing despair and exhaustion just takes over.

Try living with the fear – every time the phone would ring or the door would knock would it be the news we all dreaded? I remember once when he was missing for 3 days, and I saw two police officers come up the drive. The difference this time was one of the officers was a police women and I thought, 'this is it, they have sent a lady to give me the news'. Imagine living with fear on that level every day and night! Also came embarrassment, shame, guilt, anxiety, anger, isolation, despair and feeling powerless. I had lost both my parents and had no time to grieve; I was trying to keep the family together, trying to cope with my son's needs and the drinking, trying to get someone to really listen, trying to find the energy to get out of bed because of my own illness and it felt overwhelming every day.

Over the years my husband also suffered with depression and began to use alcohol to escape the problems. For 2 years I had to deal with both my son and husband, and eventually I had to leave my home, which did not feel secure, to stay with a friend. My marriage was in jeopardy after 31 years and my husband was on the edge of a complete breakdown. Thankfully, after I left, my husband decided to get help and stopped drinking. Four months later I returned back to my home.

My eldest son also had to receive treatment for depression; his life was affected enormously in a whole variety of ways and it's taken time to even begin to rebuild any of the relationships. It felt impossible to give him time and support and it was difficult to enjoy the good things happening in his life. One of my happiest and yet saddest memories was his wedding, when I stood at the front of the church and gave a reading about love. The loss I felt that my youngest son was not present will always be there.

Many social occasions were cancelled, destroyed, or not even thought about. There was a complete loss of normality.

Was I a carer? My son's GP certainly did not see me as one—no information regarding any support services was ever given. Our relationship felt like a battleground. I had been taking my son to see different people since he has been 2 years old—if only someone had really listened to me regarding this. As a mother I had always known there was something not right and there were problems long before alcohol was introduced into my son's life. There were many times when my son was not drinking when a comprehensive assessment that considered his previous medical history could have taken place. It took from the first incident to last year to find a person who would listen. My son felt the same. Everyone kept blaming the drinking. In court my son said: 'I have been seeing people all my life and people listen, but nobody has really heard what I am saying'.

Treatment for my son came first by a community programme, then residential treatment at the age of 19. As a Mum I never felt included in the process in any way and it would have been very valuable to have been given information and support in my own right even if my son had not wanted me to be involved with his treatment. Recovery needs to be for the whole family. Guidance around relapse would have been especially helpful. I felt elated when my son entered residential treatment for the first time, but then felt crushed when relapse came months later.

After a period of 8 years waiting for the second attempt at residential treatment, I again felt crushed when half way through things collapsed. It goes against everything as a Mum to say 'no' to requests from your son, especially for money for a place to stay and keep safe. Imagine how hard this is! Often it is the case that no advice is given to parents of children with alcohol problems, or the advice is conflicting and many are confused as to what they should be doing to support their child. We needed help for the whole family, not help to divide us. After 2 further years of chaos, I started to try again to find someone to listen.

It was only because the mental health team would not listen to me that I requested a Carers Assessment. I felt my son was at real risk of harm to self and others and I felt it was the only way to get this fear put down in black and white, to have evidence that I had told someone. The 'merry go round' of mental health services and alcohol services nearly tipped my own balance more than once. I had medical evidence that there were underlying problems long before the alcohol addiction took hold, and I felt this was essential for correct assessment. This was a complete failure in my eyes and later I was proved right. It did not help having a Carers Assessment worker who did not have any knowledge of addiction,

The biggest help and support has been through attending 12 step meetings. I have attended Families Anonymous and also attended Al Anon. The meetings helped me focus on myself, and gave me a support network in my own right. I was not judged and felt completely understood. It was a personal development of my own, helping me to understand that there were no guarantees that my son would stop drinking, but that I needed to take care of myself. It also taught me how to look at my role in my son's addiction and to support him in a more valuable way. To even begin to stand back

when my son could die was the hardest thing to do. These meetings were a 40-mile round trip each time, so there was a large chunk of time and quite a cost involved.

I have also attended two other support groups which were not 12 step. Both of these were of different value, but I sometimes find it difficult when groups get into talking about the problems too much and focus on the other person. I needed to learn new tools on how to cope with my situation. There were also many other things I needed to know, for example, how and where to go in an emergency, and finding out about these things was as hard for me as finding the correct services for my son. There was a lack of communication, a lack of information, battles around confidentiality, and a constant struggle.

I have a couple of very close friends who supported me the best they could. That might mean when I was walking the streets in desperation and depressed myself that I could find my way to their house and there was always an open door. Alcohol addiction brought family rows and sometimes, after my Mum died, I just felt I needed somewhere to go even for a short while before returning to the chaos. The people closest to me (for example, my husband and my eldest son) were also affected and found it difficult to support me. This was a 24-hour situation and my husband had to continue to work to support the whole family and my eldest son needed to pursue his own life somehow. The main thing to do was try and support myself in my role as a carer by my own self-care.

I have attended two residential family programmes which were also very useful; however, they had to be funded by us and were costly. I attended my first family programme when my son entered treatment for the first time several years ago. I wanted to learn how to deal with the situation in a better way, and during the 3 days of the course, I was able to look at my own feelings and confirm that getting help for myself was extremely important. It also helped me to look at ways of supporting and loving my son but not to support his drinking in any way. I attended the programme alone. My second 5-day residential course was 5 years ago. It helped me learn more about addiction, look at my own self-care and understand my behaviours around my son. It helped me gain the courage to do some of the things I needed to do but were extremely difficult. I also attended this alone, whilst my husband was at work and continuing to support the family. However, one person changing can start the process of change amongst others.

Everything I have learnt and put into practice has helped me maintain my own emotional and physical health in a much more positive way today. It's taken a lot of work and courage. The biggest turning point for us all was the confirmation of underlying problems last year. My son can now understand his reasons for drinking when he does, which he has been trying to express for many years. Attitudes towards carers and family members need to change if people are to get well. You cannot have a relationship with the person's practitioner if that practitioner believes that only the person with the alcohol problem is involved. Our family spent years trying to get the right help for our son, which would have made such an enormous difference to not only his life but to all of our lives. There are no guarantees that he would still have not developed an addiction to alcohol; however, knowing that the underlying problems were real would have helped us all see things in a different light. These years are lost.

On New Year's Day this year we had our first family meal together for 10 years. Rebuilding relationships within the family is one of the main areas to restore. My son is doing well at the moment – he is working and gaining huge insight into himself. Unfortunately when there are changes in our son, things for us can change overnight, but we just have to deal with this as and when it comes. At present he is living with us, but only because of a relationship ending. At times it can still be very difficult, but clear boundaries help us all.

4.3.3 Carer account B

My partner had always been a heavy drinker and in his teens and twenties had used heroin. He came from a background of regular social drinking and his parents run a pub where he lived and served in the bar. This set a pattern of daytime and evening drinking every day. At weekends he would often drink a great deal and would be completely immobilised for at least a day with very bad hangovers and sickness. He was diagnosed with hepatitis C which had damaged/is damaging his liver and this was probably the cause of his extreme reaction to alcohol.

Reacting to pleas from us, his family, he stopped drinking every evening in the local pub but we found out later that he was drinking after work and would also buy alcohol when he took the dog for a walk later in the evening. Over time, and coinciding with a change in family life with me taking up a high pressured and senior job and our children leaving home to go to university, he began to drink far more. His behaviour was dramatic and extremely upsetting as it was obvious that he was drinking to obliterate his misery and when he did drink like this he would become tearful and abusive dependent on his mood. He never drank at home but would go to parks or drink while walking around the area until he collapsed on benches or in the park and we had to go and find him. I made him go to the doctor who called out the local mental health team who put him on a high dosage of antidepressants, but things got worse not better and he then started to disappear overnight. As the GP said, the best thing he could do was to be arrested and dry out because he couldn't get help until he presented in a sober state. The police agreed but the nightmare of disappearances, us taking turns roaming the streets looking for him, trying to entice him home via phone calls, the muggings and beatings he got whilst collapsed on the streets, went on for years. He would go to AA to keep us quiet and also went to the GP every few weeks which, looking back, was the only indication that he wasn't trying to kill himself through drink. Friends tried to help and he was offered psychotherapist support by work but he would not go and he ignored friends. The only place he could go to whilst intoxicated was a drop-in centre which, for a while, successfully engaged him and allocated him a case worker. I tried to talk to the worker to find out how we could help or what was happening but because of stringent confidentiality issues I got no help or information at all. This did not happen when drugs came into the picture and I do feel that given my partner's drunkenness, he did not understand or was given no guidance on how to opt out of the confidentiality issue.

It was the downward spiral which completely takes over someone who is vulnerable and makes me wonder about the word 'carer'. You aren't caring for someone who is in this state except by trying to keep them from harm and trying to get them to eat and sleep. Well, you start like that but by the end you are so furious that even that gets

withdrawn – a useless threat really as my partner did not care if he did not eat or if he smelt or slept in the park. The family kept ourselves to ourselves and it was dreadful to watch the effect it had on my younger child who was more vulnerable and a teenager at the time. The anger and anguish in the house was there all the time although we often tried to pretend we were a normal family watching *East Enders* together. But all the time we would be watching and waiting for him to turn up so we could relax a bit. We even tried locking him in – all these desperate tactics made no difference.

There was no one professionally who helped us in the first years and it was only when we found out by accident that my partner was back on heroin that any funded support for the family was offered. A local service for families of people with drug and alcohol problems helped us. We had a family meeting and were able to ring and talk to the key worker assigned to us. In meetings we wrote things down on flip charts and talked through lots of issues. This helped the children face up to their father and to write down their wishes for the future and their terms for us taking him back. But the support was not continued and we were led to believe that this was because he was being treated primarily as a drug user rather than as a dependent drinker and there was little funding for the latter.

I think that for my partner drink was far more pernicious than drugs. It nearly destroyed our family because of the extreme moods, the anger it caused in all of us, the tears and the disappearances. On drugs he could lead a sort of normal life – so much so that we did not even know he was taking heroin for months. He finally stopped drinking when my children and I said we had to leave or to get help. We did not realise that he had just swapped his addiction.

Families and friends find it far more difficult to deal with drink because it is so much part of our social makeup – and so available. It is impossible to stop someone drinking if they don't want to stop because they can get it at any time and it is relatively cheap. We tried a number of things but we had no support from professionals so we were sort of making it up as we went along. We made a lot of mistakes – like locking him in and attempting to forcibly remove cans and so on when he was on the streets – but we only found out why these were not useful tactics until later on. The web was informative but not personal and the family support group Al Anon was just not suitable for us, especially because the meetings were in the day time and I had a full-time job.

Eventually my partner reached rock bottom and was arrested for possession of Class A drugs. He was very drunk as well. From the moment of his arrest, all the help came pouring in – detox was arranged, community rehab set up, and a care manager appointed who worked with him on a care plan. We were also offered family therapy via these services. We did not take it up mainly because we felt we had gone through enough and we felt our coping skills and understanding of what to do next were stronger. We wanted him to go through rehab for himself. The 12-step therapy used by the rehab service helped him a lot and he started going to AA and NA several times a week. He has not had a drink – except for a few pretty dreadful slips – for nearly 3 years and has not used heroin. But when you are involved like this with a user, you are always on the lookout for slips or lapses. Ironically it would be better if such a lapse

was drug related as I am still not at all sure where we would get the same support if he started drinking again.

Being a 'carer' of a dependent drinker is lonely, frustrating and terribly tragic—tragic because the thing you learn is that you know if someone wants to drink and stay drunk, they can always find a way. Street culture becomes their family and the real family are left outside.

4.4 Review of the qualitative literature

4.4.1 Introduction

A systematic search for published reviews of relevant qualitative studies of people who misuse alcohol was undertaken. The aim of the review was to explore the experience of care for people with alcohol problems and their families and carers in terms of the broad topics of receiving a diagnosis, accessing services and having treatment.

4.4.2 Clinical questions

For people who misuse alcohol, what are their experiences of having problems with alcohol, of access to services and of treatment?

For families and carers of people who misuse alcohol, what are their experiences of caring for people with an alcohol problem and what support is available for families and carers?

4.4.3 Evidence search

Reviews were sought of qualitative studies that used relevant first-hand experiences of people with alcohol problems and families/carers. For more information about the databases searched see Table 1.

Table 5: Databases searched and inclusion/exclusion criteria for clinical evidence.

Electronic databases	CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	Systematic reviews and narratives of qualitative studies, qualitative studies
Population	Individuals with alcohol dependence or harmful alcohol use, families and carers of these individuals, staff who work in alcohol services
Outcomes	None specified - any narrative description service user experience with alcohol problems

4.4.4 Studies considered

Based on the advice of the GDG, this review was focused on qualitative research only as it was felt it was most appropriate to answer questions about the experience of care of those with alcohol dependence or alcohol misuse. As good quality qualitative research exists within the literature, quantitative and survey studies were excluded.

The search found 30 qualitative studies which met the inclusion criteria (Aira *et al.*, 2003; Allen *et al.*, 2005; Bacchus *et al.*, 1999; Beich *et al.*, 2002; Burman, 1997; Copeland, 1997; Dyson, 2007; Hartney *et al.*, 2003; Hyams *et al.*, 1996; Jethwa, 2009[5]; Kaner *et al.*, 2008; Lock *et al.*, 2002; Lock, 2004; Mohatt *et al.*,2007; Morjaria & Orford, 2002; Nelson-Zlupko *et al.*, 1996; Nielsen, 2003; Orford *et al.*, 1998; Orford, 2003; Orford *et al.*, 2005; Orford *et al.*, 2006; Orford *et al.*, 2009; Rolfe *et al.*, 2005; Rolfe, 2009; Smith, 2004; Vandermause & Wood, 2009; Vandevelde *et al.*, 2003; Vandermause, 2007; Vargas & Luis, 2008; Yeh *et al.*, 2009).

Thirty four studies were considered for the review but they did not meet the inclusion criteria (Amiesen, 2005; Brown, Kranzler & Del Boca, 1992; Bargiel-Matusiewicz & Ziebaczewska, 2006; Happell *et al.*, 2002; Chan *et al.*, 1997; Cunningham2009; De Guzman *et al*, 2006;De Maeyer *et al.*, 2008; Grant1997; Giovazolias & Davis, 2005; Grebot, Coffinet & Laugier, 2008; Hoerter *et al.*, 2004; Kahan *et al.*, 2004; Kaner *et al.*, 1999; Karel *et al.*, 2000; Koski-Jannes, 1998; Laudet, 2003; MacDonald *et al.*, 2007; Mackenzie & Allen, 2003; Miller, Thomas & Mallin, 2006; Orford *et al.*, 2009; Pettinati *et al.*, 2003;Pithouse1996; Rychtarik *et al.*, 2000; Sellman1996; Strobbe *et al.*, 2004; Swift *et al.*, 1998; Thomas & Miller, 2007; Tonigan *et al.*, 2000; Tucker *et al.*, 2009; Vuchinich & Tucker, 1996; Wells, Horwood & Fergusson, 2007; White *et al.*, 2004; Wild *et al.*, 1998) the most common reasons for exclusion were that alcohol was not the primary substance used; or there was not a high enough percentage of people who were alcohol dependent or reaching harmful levels of alcohol consumption; or the studies were quantitative or surveys.

The characteristics of all the studies reviewed in this section have been summarised in Appendix 16a. The included studies have been categorised under six main headings: service user experience of alcohol problems, access and engagement, service user experience of assessment and treatment for alcohol problems, experience of recovery, carer experiences and staff experiences.

4.4.5 Service user experience of alcohol problems

One of the main themes that emerged under the heading of 'service user experience of alcohol problems' was reasons for discontinuation of drinking. There were seven studies (Burman, 1997; Hartney *et al.*, 2003; Jethwa, 2009; Mohatt *et al.*, 2007; Nielsen, 2003; Rolfe *et al.*, 2005, Yeh *et al.*, 2009) that looked at people's motivation for stopping drinking in populations of people who drank heavily and were untreated. All studies mentioned that a significant motivation to discontinue drinking stemmed from external factors such as relationships, employment and education. Responsibility for others was a particular catalyst in maintaining motivation to stop drinking (for example, having a child, loss of a family member, divorce or separation from a partner).

Rolfe and colleagues (2005) found that participants specified three key reasons for decreasing alcohol consumption. The first was 'needing to' decrease their alcohol

[5] It should be noted that the Jethwa (2009) paper was published, however the qualitative patient interviews accompanying them were not, and were received from a member of the GDG. The review team received written permission from the author to use the interviews to identify any themes relevant to this section.

consumption in order to minimise harm once there was a realisation that alcohol was having a direct negative impact on their emotional and physical well-being. Both Rolfe *et al.* (2005) and Burman (1997) reported that the onset of physical problems was a significant motivation to stop drinking: *'you need that scare to do it… you don't pack it in until you've had that scare and reached rock bottom*'. The second reason was 'having to' decrease alcohol consumption due to work or relationship factors. The third was 'being able to cut down', which referred to no longer feeling the need or desire to consume alcohol, and was typically inspired by a positive or negative change in a specific area of their life (for example, medical treatment or change in employment).

In the qualitative component of their study, Hartney *et al.,* (2003) found that most participants did not have a sense of being unable to stop drinking alcohol, and issues such as relationships or driving a car would be prioritised over continuing to drink. This furthers the idea that for untreated heavy drinkers, triggers and cues for alcohol consumption are largely socially determined. Another interesting finding was the conscious process many participants went through in order to find moderation strategies to apply to their alcohol consumption. This was largely based around an observation of their own drinking in relation to other people's drinking levels, and disconnecting themselves from a drinking 'taboo' or what they considered to be 'dependence', including concealing evidence of alcohol consumption or the effects of physical withdrawal.

Nielsen (2003) found that participants in Denmark used different ways to narratively describe and contextualise their drinking behaviour. Several participants categorised their alcohol consumption as 'cultural drinking', where alcohol was used in a social and cultural context. Cultural drinking is a way of normalising alcohol consumption within a social environment (such as drinking at a party). Moreover, participants in this study distinguished their own heavy alcohol consumption from what they perceived as 'real alcoholics', who appeared to be more out of control: *'Real alcoholics are drinking in the streets'*.

Other patterns of drinking included symptomatic drinking, where patients drink as a reaction to external influences (for example, workload or relationship difficulties) or internal influences (for example, mental health problems). Cultural drinkers were found to use therapy and treatment more for information and feedback, rather than for the helpfulness of their therapists. Cultural drinkers tended to reply on their own willpower to cut back on their drinking. Conversely, those who were symptomatic drinkers used alcohol more as a way to solve problems and were more reliant and engaged in their treatment sessions with their therapists. Lastly, the Nielsen (2003) study highlights the process of heavy drinking and the 'turning point' that many harmful and dependent drinkers experience once the realisation is made that their alcohol consumption needs to change and treatment is needed. This turning point is in line with what Burman (1997) and Mohatt *et al.,* (2007) found as well, in that participants typically experience an accumulation of negative alcohol related events, and this prompts the decision to give up drinking. A period of reflection regarding their alcohol problems may follow, and a key event often precipitates the motivation to stop drinking, and leads to a turning point.

Recently, Jethwa (2009) interviewed service users who were alcohol dependent and found that six of the 10 participants interviewed started drinking in response to a stressful life event (e.g. depression, bereavement, or breakdown of a relationship). Other common reasons included familial history of drinking, being lured in by social networks, or just liking the taste of alcohol. Interestingly, once the decision was made to quit drinking, nearly all of the participants did not find it difficult once this 'turning point' was reached.

Yeh and colleagues (2009) conducted a study to look into the process of abstinence for alcohol-dependent people in Taiwan and discuss their challenges in abstaining from alcohol. Based on previous theories and the interviews, Yeh and colleagues (2009) identified a cycle of dependence, comprising the stages of indulgence, ambivalence and attempt (IAA). In the first stage of indulgence, alcohol-dependent people feel a loss of control over their alcohol consumption, and in order to overcome unpleasant physical or mental states, they consume more alcohol, exacerbating their dependence:

> *'When I had physical problems and saw the doctor, they never got better. But I felt good when I had a drink. I started relying on alcohol and started wanting to drink all the time. Drinking would help me feel better'.*

In the ambivalent stage, people want to seek help but the will to drink is stronger than to remain abstinent. In the attempt phase, people try to remain abstinent but due to a lack of coping strategies in situations that trigger alcohol consumption, many relapse.

Dyson (2007) found that recovery from alcohol dependence arose from a culmination or combination of consequences, coupled with the realisation that life was unbearable as it was:

> *"My real recovery began when I admitted that my life had become unmanageable and that I could not control the drink. I experienced a deep change in thinking – sobriety had to be the most important thing in my life".*

Several participants pointed out that their decision to pursue recovery and abstinence had to be made on their own and could not be made or influenced much by others: *'It was something I had to do on my own and I had to do it for me, not for anyone else'.* Evidently this personal decision has important implications for the carers around them. The key to begin recovery appears to be the individual's willingness and readiness to stop drinking (Dyson, 2007).

An earlier study by Orford *et al.* (1998) looked at social support in coping with alcohol and drug problems at home, using a cross-cultural comparison between Mexican and English families. The main cross-cultural differences were that positive social support for Mexican relatives stemmed mostly from family; whereas English relatives mentioned self-help sources, and professionals and friends in addition to family. The accounts from the participants mentioned family and friend support as more unsupportive or more negative for the English families. Conversely, the Mexican families often mentioned their family and neighbours as significant contributors of support. The researchers explored the participant's perceptions of the positive and negative drawbacks to their heavy drinking. The negative aspects included increased

vulnerability to arguments and fights, and the unpleasant physical effects of drinking (such as waking up tired, stomach upsets and headaches). Many participants mentioned the adverse effects alcohol had had on their physical and mental health. Interestingly, several participants mentioned drinking in order to cope with difficult life events, but masked this association with coping and alcohol by terming it being 'relaxed'. Many submerged the notion of coping by using the fact that alcohol helped them relax in distressing situations. Thus, the long-term psychological and short-term physical consequences were noted as the principle drawbacks of harmful alcohol consumption, whereas coping, feelings of being carefree and relaxed, seem to constitute the positive aspects of drinking.

4.4.6 Access and engagement

In the review of the qualitative literature, several themes emerged under the broad heading of 'access and engagement' to services for alcohol problems, including the factors that may act as barriers to accessing treatment services, such as external and internal stigma, ethnicity and gender. This review also identified 'reasons for seeking help' as a theme emerging from the included studies. There were 8 studies from which themes of access and engagement emerged (Vargas *et al.,* 2008; Dyson, 2007; Lock *et al.,* 2004, Vandevelde *et al*., 2003; Vandermause & Wood, 2003, Nelson-Zlupko *et al.,* 1996; Copeland, 1997; Rolfe *et al.,* 2009; Orford *et al*., 2006).

Stigma

Dyson (2007) found that all participants used strategies to hide their alcohol dependence, including covering up the extent of their alcohol consumption. This was primarily due to the fear of being judged or stigmatised: *'I knew that I was ill but was too worried about how other people would react. I felt I would be judged…'* All participants in the study had some contact with healthcare professionals in an attempt to control or reduce their drinking. GPs were described as being particularly helpful and supportive, and nurses and other healthcare workers as less understanding and more dismissive, especially those in accident and emergency departments; this contrasts with another study [Lock *et al.,* 2004], where people with alcohol problems found primary care nurses to be helpful.

Ethnicity

Vandevelde and colleagues' (2003) study of treatment for substance misuse looked at cultural responsiveness from professionals and clients' perspectives in Belgium. People from minority groups found it difficult to openly discuss their emotional problems due to cultural factors, such as cultural honour and respect. Participants stressed the absence of ethno-cultural peers in substance misuse treatment facilities, and how this made it hard to maintain the motivation to complete treatment. Although this study had a focus on substance misuse (that is, both drugs and alcohol), it is important to note its generalisability to alcohol services and treatment.

Gender

Vandermause and Wood (2009) and Nelson-Zlupko and colleagues (1996) both looked at experiences and interactions of women with healthcare practitioners in the United States. Many women described waiting until their symptoms were severe before they would seek out healthcare services:

> *'…it's hard for me to go in… and it's not someplace that I want to be, especially when I know that I have to be there. I know that I'm ill, I don't' want to admit it… I have to get my temperature taken and my blood pressure and they gotta look at my eyes and my ears… find out what it is that I've got from somebody else sharing a bottle you know.'*

Once the women sought help from a healthcare professional, several felt angry and frustrated after repeated clinic visits resulted in being turned away, treated poorly, or silenced by comments from healthcare professionals. Some women would go in needing to be treated for a physical health problem, and the practitioner would address the alcohol problem while ignoring the primary physical complaint.

Conversely, other women were satisfied about how they were treated in interactions with their practitioners, which influenced perceptions of the healthcare services, seeking out treatment, and feeling comfortable about disclosing their alcohol problems:

> *'I was confused and angry, and the doctor made me feel comfortable, even though I was very very ill… he let me know that I was an individual person but I had a problem that could be arrested. He was very compassionate very empathetic with me and told me the medical facts about what was happening to m e, why I was the way I was and he told me a little bit about treatment, what it would do…so I was able to relax enough and stop and listen rather than become defensive…'*

When women specifically sought treatment for their alcohol problems, the authors suggested that there was a crucial need for healthcare practitioners to make the patient feel comfortable and acknowledge their alcohol problem in addition to addressing any other physical health problems.

Nelson-Zlupko and colleagues (1996) found that individual counselling might be important in determining whether a woman is retained or drops out of treatment. Many women felt that what they wanted from treatment was someone to 'be there for them' and lend support. A therapist's ability to treat their patients with dignity, respect and genuine concern was evaluated as more important than individual therapist characteristics (such as ethnicity or age). Some women mentioned that good counsellors were those who:

> *"…view you as a person and a woman, not just an addict. They see you have a lot of needs and they try to come up with some kind of a plan."*

Both Nelson-Zlupko and colleagues (1996) and Copeland (1997) highlighted that childcare was a particular need for women as it was not widely available in treatment. When childcare was available, this was perceived to be among one of the most helpful services in improving attendance and use of treatment and drug/alcohol services. In addition, women felt strongly about the availability and structure of outpatient services offered and felt there should be more flexible outpatient programmes taking place in, for example, the evenings or weekends.

Copeland's (1997) Australian study was of women who self-managed change in their alcohol dependence and the barriers that they faced in accessing treatment. One of the

central themes of the study was the social stigma that women felt as being drug or alcohol dependent. Seventy-eight percent of participants felt that women were more 'looked down upon' as a result of their drinking, and the additional burden of an alcohol or drug problem only increased the stigma. Some women reported that the feeling of being stigmatised impacted on their willingness to seek treatment:

> *'There is the whole societal thing that women shouldn't show themselves to be so out of control … that stigma thing was part of the reason for not seeking treatment.'*

In line with this, Rolfe and colleagues (2009) interviewed women in the UK about their perceptions of their heavy alcohol consumption and its relation to a wider social perspective. Many women claimed that stigma was a major obstacle to accessing treatment services, and that while men did carry stigma as heavy drinkers, there was an additional stigma for women due to the way a 'heavy drinking woman' was perceived within society. The interviews emphasised that women need to perform a 'balancing act', in order to avoid being stigmatised as a 'manly' woman or as an addict. These discourses are important in understanding the perception of gender differences in heavy alcohol consumption and ways in which stigma can affect women and their ability and willingness to seek treatment for their alcohol problems.

Reasons for seeking help

A study conducted by Orford and colleagues (2006) investigated the reasons for entering alcohol treatment in the UK. The study was based on pre-treatment interviews from participants who were about to commence the UK Alcohol Treatment trial, and receive either motivational enhancement therapy (MET) or social behavioural network therapy (SBNT) for alcohol dependence or harmful alcohol use. Reasons for entering alcohol treatment included the realisation of worsening problems and accumulating multiple alcohol problems, which had a negative impact on both family members and the participants' health. Participants were also interviewed about reasons for seeking professional treatment as opposed to unaided or mutual self-help. Common reasons for seeking formal help included such help being suggested by primary care workers, a strong belief in the medical model and in counselling or psychological therapy, or feelings of helplessness.

Accessing help: Reasons and preferences

Lock *et al.* (2004) conducted a focus group study with patients registered with general practices in England. Participants were classified as "sensible" or "heavy/binge drinkers". Participants responded positively to advice delivered in an appropriate context and by a healthcare professional with whom they had developed a rapport. Overall, the GP was deemed to be the preferred healthcare professional with whom to discuss alcohol issues and deliver brief alcohol interventions. Practice nurses were also preferred due to the perception that they were more understanding and more approachable than other healthcare workers. Most said they would rather go straight to their GP with any concern about alcohol, either because the GP had a sense of the patient's history, had known them for a long time or because they were traditionally whom the person would go to see. It was assumed the GP would have the training and experience to deal with the problem, and refer to a specialist if necessary. Alcohol workers were perceived by many as the person to go to with more severe alcohol

problems as they were experts; but this also carried the stigma of being perceived to have a severe alcohol problem. Seeing a counsellor was also perceived as negative in some ways, as there would be a stigma surrounding mental health problems and going to therapy.

4.4.7 Service user experience of assessment and treatment for alcohol problems

In the review of the qualitative literature, several themes emerged under the broad heading of 'service user experience of treatment for alcohol problems', including experience of assessment (pre-treatment), of assisted withdrawal, of other treatments (such as psychological interventions), and of treatment setting (inpatient). In this review of assessment and treatment, there were 6 studies included (Hyams *et al.,* 1996, Orford *et al.,* 2005; Orford *et al*., 2009; Allen *et al.,* 2005; Smith, 2004; Bacchus *et al.,* 1999; Dyson, 2007).

Experience of assessment (pre-treatment)

Hyams and colleagues (1996) interviewed service users about their experience and satisfaction with the assessment interview prior to engagement in alcohol treatment. The study had both a quantitative and qualitative aspect to it. The qualitative component assessed the best and worst aspects of the assessment interview. Thirty-three of the 131 participants said that the therapeutic relationship with the interviewer was most beneficial (as assessed by 'The interviewer's understanding of the real me', 'Friendliness of the interviewer' and 'A feeling of genuine care about my problems'). Twenty participants appreciated the ability to talk generally and therapeutically to the interviewer about their problems. Eight participants reported that the assessment interview provided them with a sense of increased awareness about their alcohol problems and its impact on their lives: *'I found insight into why I drink…'* Others found that the assessment interview was crucial in taking the first step into treatment: *'Glad that I did attend the interview'* and *'Given me some hope'*.

The drawbacks of the interview were few from the participant's perspective, which included nervousness generally and specifically about starting the interview itself. Some criticised the interviewer for not giving enough feedback or not having enough time to talk. Several participants felt that it was distressing to have to reveal so much information about their drinking problems, and come to a state of painful awareness about their problem. This study is noteworthy because it highlights the importance of a thorough assessment prior to entering alcohol treatment that allows participants to speak freely to an accepting, empathetic interviewer, and which, if a positive experience for the service user will increase engagement and motivation to change in subsequent alcohol treatment programmes.

In line with these findings, Orford and colleagues (2005) found that a comprehensive pre-treatment assessment was perceived by participants to have motivational and self-realising aspects to it. Many participants expressed that this assessment was influential in increasing motivation to undergo their alcohol treatment.

Experience of assisted withdrawal

Two studies, Allen and colleagues (2005) and Smith (2004) captured the patient experience of medically-assisted withdrawal programmes for alcohol problems in both the UK and Australia. Both studies found that participants expressed fears about the future and a hesitation about coping with life events that were previously associated with alcohol consumption:

> *'I feel safe in the environment but I don't feel safe with my thoughts at the moment because I can't use alcohol or any drug to cope with it….'*

The most common themes emerged around fears regarding social environment, the physical effects of withdrawal, and medication prescribed during detoxification. Participants discussed fears about returning to their homes after detoxification, and how to lead a life without alcohol:

> *'When you've done the first few days [of detoxification], you get your head back together and start to think, How am I going to be able to cope outside? You know you've got to leave here sometime, so how am I going to cope?'*

Participants also expressed significant concerns about the effects of medication, although there were also a number of positive experiences of medication which were referred to but were not described in detail. Some participants feared that their medication would be addictive:

> *'I didn't want another problem of having to get off something as well as the booze. I was worried that I could get addicted to the tablets as well and then start craving for those'.*

Nearly all participants were apprehensive about the transmission of information about medication between the staff and themselves; they felt they had inadequate information about what medication they were taking, why they were taking it, and the effects it may have on them:

> '*I didn't know what they were, what they were going to do to me… they didn't tell me why I was taking them'.*

It is clear from this study that providing adequate information about assisted withdrawal and medication procedures needs to be ensured in alcohol services.

A significant proportion of participants also expressed fears about the physical effects of withdrawal, and any pain and/or distress that may be a side effect of the detoxification programme. Those who had had previous medically-assisted withdrawals prior to this study seemed to have the greatest fears. Lastly, participants discussed fears about their future and were concerned about their ability to cope once completing the detoxification programme. These fears mostly stemmed from difficult interpersonal situations and coping strategies:

> *'I'm worried about having too much time on my hands; the day goes so much quicker with a few drinks inside you'.*

In both studies service users expressed a lack of confidence and an inability to resist temptation; they also felt that they were not being accepted back into their original

social networks where heavy drinking was perceived as the norm. Additionally, fears about the future were related to a feeling that the hospital setting was too far removed from real life:

> *'It's nice and safe in here. You are secure in here. But it's not real life is it? And it tells you nothing about how you are going to cope when you are back in the same old situations with the same old problems'.*

Participants in the Smith (2004) study also articulated feelings of being out of control during their admission to treatment. These feelings of distress revolved around the difficulty to alter their alcohol consumption, and stick to a reduced consumption level or abstinence:

> *'You get well physically and you start thinking clearly… you start telling yourself you're over it… you might maintain some kind of normal drinking activity for a short period of time. I just believe that I can't keep doing it. I don't want to'.*

With each medically-assisted withdrawal, the goal of abstinence seemed more distant—the thought of this was anxiety-provoking for many participants as they felt they would be unable to maintain abstinence in the future. After medically-assisted withdrawal, they would have to return to a life where all their personal, professional and relationship difficulties still existed but were previously associated with alcohol.

Conversely, there were positive feelings about treatment, as most felt they had taken steps to bring about positive changes in their lives by seeking treatment. The facility enabled participants to have respite from their lives as well as social and emotional support from other participants in the programme. The authors suggested that nurses could assist participants in reducing negative feelings (such as shame) by closely observing behaviour and being more sensitive and empathetic to service users' feelings, thereby strengthening therapeutic communication between staff and patients.

Experience of psychological treatment

Orford and colleagues (2005, 2009) carried out a content analysis of service users' perspectives on change during a psychological intervention for their alcohol dependence in the UK Alcohol Treatment Trial (UKATT). Participants highlighted that psychological treatment had helped them to think differently, for example about fearing the future and focusing on the downside of drinking. Others talked of adopting a more positive outlook or more alcohol-focused thinking (for example, paying attention to the physical consequences such as liver disease or brain damage). Several participants mentioned that*: 'the questions, the talking, being honest, being open – that was positive [of treatment]'*. Other factors to which change was attributed to were awareness of the consequences of drinking, and feeling comfortable talking about their alcohol consumption.

Experience of support from family and voluntary organisations

Orford *et al.* (2005) also found that the influence of family and friends helped in promoting change in alcohol consumption. Treatment seemed to assist participants in finding non-drink related activities and friends, and seeking out more support from their social networks to deal with problematic situations involving alcohol. Supportive

networks provided by AA and the 12-step programme facilitated recovery for participants in the Dyson (2007) study as well, as they were able to be with others who genuinely understood their experiences and fostered a sense of acceptance: *'Here was a bunch of people who really understood where I was coming from'.*

Experience of treatment setting – inpatient

Bacchus *et al.* (1999) carried out a study about opinions on inpatient treatment for drug and alcohol dependence. Over a third of participants reported that they would have preferred to enter treatment sooner, because there was an urgent need to maintain treatment motivation and receive acute medical care:

> *'When you make that decision to ask for help, you need it straight away. If you have to wait a long time to get in you just lose your motivation and you might just give-up.'*

Participants also felt frustrated about the lack of communication and liaison from the referring agency during the waiting period. The structured individual and group counselling treatment programme was seen as a generally effective way of improving self-confidence and self-esteem. Educational group discussions about substance use and risks were particularly positively regarded. Recreational groups (for example, art therapy, exercise and cookery) also proved to be beneficial in terms of engaging in other non-drink related activities. One of the most positive aspects of treatment noted by participants was the quality of the therapeutic relationships. Staff attitudes, support, being non-judgemental and empathetic were all mentioned as crucial components of a positive experience in treatment. Sixty-two percent of patients had made prior arrangements with staff for aftercare treatment, and expressed satisfaction with the arrangements. The only exception was that patients wished for more detailed information about the next phase of their treatment.

4.4.8 Experience of recovery

Four studies (Burman, 1997; Mohatt *et al,* 2007; Morjaria & Orford, 2002; Yeh *et al*., 2009) looked at the experience and process of recovery for people with alcohol problems. All studies with the exception of Yeh *et al.,* (2009) looked at recovery from the standpoint of drinkers who were untreated. Nearly all the studies highlighted the importance of utilising active coping and moderation strategies in order to stop consuming alcohol, and a number of the studies touch on the importance of positive social support networks, faith and self-help groups.

Morjaria and Orford (2002) examined the role of religion and spirituality in promoting recovery from drinking problems, specifically in AA programmes and in South Asian men. Both South Asian men and men in AA began recovery where there was a feeling of hitting 'rock bottom' or reaching a turning point where they felt their drinking must stop. Both groups drew on faith to help promote recovery, but the South Asian men already had a developed faith from which to draw upon, whereas the AA men had to come to accept a set of beliefs or a value system and develop religious faith to help promote abstinence.

In terms of self-recovery strategies, participants in Burman (1997), Yeh *et al.,* (2009) and Mohatt *et al.,* (2007) often utilised recovery strategies that mirrored those in formal treatment, consisting of drawing on social support networks and avoiding alcohol and

alcohol-related situations. Seeing another person giving up alcohol also helped to promote abstinence and motivation, again highlighting the necessity of positive support networks. Another stage of sobriety for participants in Mohatt's study (2007) involved a more gradual acceptance of their vulnerability towards consuming alcohol and continuing to strategise and resist the urge to drink. Additional coping strategies outlined by Burman (1997) were setting a time limit for recovery; discussing their goals and plans with others to help keep them on track; and keeping reminders of negative experiences in order to help prevent further relapse.

Similar to those in formal treatment programmes, once in the midst of self-recovery, participants reported a number of positive changes since abstaining (for example, increased energy and memory, self-awareness and empowerment), and more external benefits including regaining trust from their social networks and reintegrating into society. Negative consequences of abstinence included edginess and physical side effects, family problems, struggles with craving and a loss of a specific social circle or group previously related to alcohol.

Taken together, the self-recovery studies highlight the process of abstinence for alcoholics, stressing that the path is not straightforward, and assistance from self-help groups and social support networks are crucial to help ensure a better recovery.

4.4.9 Carer experiences

Four studies (Gance-Cleveland, 2004; Murray, 1998; Orford *et al.,* 1998; Orford *et al*., 2003;) were found that could be categorised under the heading 'carer experiences'.

Orford *et al.,* (1998) conducted cross-sectional interview and questionnaire studies with a series of family members in two sociocultural groups in Mexico City and in the west of England. They found that there were three approaches to interacting with their family members with alcohol problems: (1) tolerating, (2) engaging, and (3) withdrawing. In the first approach, the carer would tolerate inaction and support the person in a passive way. Some carers mentioned taking the 'engaging' position with their family members in an attempt to change unacceptable and excessive substance use. Some forms of engagement were more controlling and emotional in nature; others more assertive and supportive. Lastly, some carers mentioned emotionally and physically withdrawing from their family members with an alcohol problem (e.g. asking their family member using alcohol to leave the house). This was seen as a way to detach oneself from the alcohol problem of their family member. One form of coping that carers also mentioned was that one needs to enforce supportive and assertive coping:

> *'You need to be very strong, to be there and talk to him but still stick to your own values and beliefs in life'.*

There was significant overlap between the coping strategies outlined by both families from England and from Mexico. Families in both countries used assertive and supportive ways of coping with their family member's alcohol problem, either through direct confrontation, financial or emotional sacrifice.
Thus, even given a different sociocultural context, there are several common ways for carers to cope and interact with a family member with an alcohol problem.

Orford and colleagues (2003) interviewed the close relatives of untreated heavy drinkers. Most relatives recognised the positive aspects of their family member consuming alcohol (for example, social benefits), and reported a few drawbacks to drinking. Many family members contrasted their family member's current problem with how their problem used to be. Other family members used controlling tactics (for example, checking bottles) as a way to monitor their family members, while others tried to be tolerant and accepting of their family member's drinking behaviour.

There are two qualitative studies that have looked at the perspectives and experiences of people whose parents misuse alcohol. Murray (1998) conducted a qualitative analysis of five in-depth accounts of adolescents with parents who misuse alcohol and found four main themes that corroborate the qualitative analysis conducted for this guideline (see Section 1.6). The themes comprised: 1) 'The nightmare', which includes betrayal (abuse/abandonment), over-responsibility, shame, fear, anger, lack of trust and the need to escape; 2) 'The lost dream'- which consists of loss of self-identity and loss of childhood (lack of parenting, comparing what one has done to others, unrealistic expectations); 3) 'The dichotomies', which is the struggle between dichotomies, for example, love and hate (towards parents), fear and hope (towards the future) and denial and reality; 4) 'The awakening', which is gaining an understanding of the problem, realising alcohol is not an answer (possibly through their own experiences), realising they were not to blame and regaining a sense of self.

Another qualitative study (Gance-Cleveland, 2004) investigated the benefit of a school-based support group for children with parents with alcohol problems and found that the group helped them to identify commonalities with each other, feel that they were understood, support and challenge each other, and share coping strategies. The children who took part also felt that the group was a trusted and safe place in which they could reveal secrets and feel less isolated and lonely, that it enabled them to be more aware of the impact of addiction on family dynamics, and helped them increase resilience and do better at school (Gance-Cleveland, 2004). This study also supports the findings found in the qualitative analysis in Section 1.6, in that talking to others (especially with those who have had similar experiences) was found to be helpful in terms of coping, making friendships and understanding more about alcohol problems.

4.4.10 Staff experiences

There were six studies (Aira *et al.,* 2003; Beich, *et al.,* 2002; Kaner, *et al.,* 2008; Lock, *et al.,* 2002; Vandermause, 2007; Vandevelde *et al.,* 2003, Vargas & Luis, 2008) looking at the experience of staff who work with people with alcohol problems. There were several themes emerging from staff experiences, the first being hesitancy in delivering brief interventions to people with alcohol problems. Staff implementing the WHO screening and brief intervention programme in Denmark found that it was difficult to establish a rapport with patients who screened positive for alcohol problems and ensure compliance with the intervention (Beich *et al.,* 2002). In England, primary care practitioners had little confidence in their ability to deliver brief interventions and override negative reactions from patients (Lock, 2002). Furthermore, because alcohol misuse can be a sensitive and emotional topic, a significant proportion of the staff in the studies expressed a lack of confidence about their ability to counsel patients effectively on lifestyle issues (Aira *et al.,* 2003; Beich *et al.,* 2002; Lock *et al.*, 2002):

> *'…the patient does not bring it up and obviously is hiding it… [alcohol]…It is a more awkward issue; which of course must be brought up…'*

Approaching emotional problems related to substance misuse through the medical dimension might facilitate the treatment of minority groups, since it was perceived that emotional problems were more often expressed somatically (Vandevelde *et al*., 2003).

A positive experience with a service user involved an assessment using effective diagnostic tools where staff were able to employ an indirect, non-confrontational approach and service users were able to discuss their problems and tell their story at their own pace (Vandermause, 2007).

Both Beich *et al.,* (2002) and Lock *et al.,* (2002) highlighted that brief interventions and confronting service users regarding their alcohol consumption was important; there were, however, a number of significant barriers to delivering these interventions effectively, for example, the fear of eliciting negative reactions from their patients. Staff interviewed in the Vandermause (2007) qualitative study also found that staff had concerns about defining alcohol as problematic for their patients.

Aira *et al.,* (2003) found that staff were not ready to routinely inquire about alcohol consumption in their consultations, unless an alcohol problem was specifically indicated (for example, the service user was experiencing sleeplessness, high blood pressure or dyspepsia). Even when they were aware of alcohol problems in advance, staff still had significant difficulty in finding the ideal opportunity to raise the issue with their patients. If they did not know in advance about a drinking problem, they did not raise the issue.

Kaner and colleagues (2008) looked at GPs' own drinking behaviour in relation to recognising alcohol-related risks and problems in their patients. The interviews indicated that GPs' perceived their own drinking behaviour in two ways. Some GPs drew on their own drinking behaviour when talking to patients, as it could be seen as an opportunity to enable patients to gain insight into alcohol issues, facilitate discussion, and incorporate empathy into the interaction. Other GPs separated their own drinking behaviour from that of 'others', thereby only recognising at-risk behaviours in patients who were least like them.

Vargas & Luis (2008) interviewed nurses from public district health units in Brazil, and discovered that despite the fact that alcoholism is perceived as a disease by most of the nurses, the patients with alcohol problems who seek treatment are still stigmatised:

> *'We generally think the alcohol addict is a bum, an irresponsible person, we give them all of these attributes and it doesn't occur to you that [he/she] is sick'.*

Furthermore, the nurses interviewed seemed to express little hope and optimism for their patients, as they believed that after being assisted and detoxified, they would relapse and continue drinking:

'…he comes here looking for care, takes some glucose and some medications, and as soon as he is discharged he goes back to the back to drink'.

This study highlights the extent of external stigma that those with alcohol problems can face within the healthcare setting, and how it could prevent positive change due to an apprehension about continually accessing services or seeking help.

All six studies made recommendations for improving staff experience when engaging with people with alcohol problems, with an emphasis on training, communication skills and engaging patients about alcohol consumption, combined with a flexible approach to enhance dialogue and interaction. However, although many healthcare professionals received training about delivering brief interventions, many lacked the confidence to do so and questioned their ability to motivate their patients to reduce their alcohol consumption. Staff also frequently cited a lack of guidance concerning alcohol consumption and health. Clear health messages, better preparation and training, and more support were cited as recommendations for future programmes. As many healthcare professionals found screening for excessive alcohol use created more problems than it solved, perhaps improving screening procedures could improve the experience of staff delivering these interventions.

4.4.11 Summary of the literature

The evidence from the qualitative literature provides some important insights into the experience of people with alcohol problems, their carers and staff. Problematic alcohol consumption appears to stem from a range of environmental and social factors, including using alcohol to cope with stressful life events, having family members with alcohol or drug problems, and/or social situations which encourage the consumption of alcohol. A cycle of dependence then begins wherein the person goes through stages of indulgence, ambivalence, and attempt, resulting in a loss of control over their alcohol consumption. This leads consumption of more alcohol to counteract unpleasant physical or mental states. As the alcohol consumption becomes harmful, there seems to be an accumulation of negative alcohol-related events. These can become the catalyst for change in the person's life when the person realises that their alcohol problem requires further assistance and/or treatment. This readiness or willingness to change needs to be determined first by the person with alcohol problems, or with the support and insight from their social networks—readiness to change cannot be imposed externally. These differing patterns of alcohol consumption and reasons for deciding to engage in treatment or change one's behaviour mean that treatment services need to understand an individual's reasons for drinking and how this may influence treatment.

With regards to access and engagement in treatment, once people with alcohol problems had made the conscious decision to abstain from or reduce their drinking, they were more willing to access treatment. Barriers to treatment included internal and external stigma, an apprehension towards discussing alcohol-related issues with healthcare professionals, and a fear of treatment and the unpleasant effects of stopping drinking. As a group, women felt that they faced additional barriers to treatment in the form of more social stigma, and the need for childcare while seeking and undergoing treatment. In addition, women felt that they received less support from treatment

providers, and would benefit from a more empathetic and therapeutic approach. The studies focusing on women and alcohol problems emphasise that a non-judgemental atmosphere in primary care is necessary in order to foster openness and willingness to change with regards to their alcohol problems.

In one study looking at the impact of ethnicity and culture on access to treatment, participants from an ethnic minority report having mostly positive experiences with healthcare practitioners, but improvements could be made to the system in the form of more ethno-cultural peers and increased awareness of culture and how it shapes alcohol consumption and misuse.

The literature strongly suggests that assessments that incorporate motivational cues are crucial in ensuring and promoting readiness to change early on in the treatment process. Having open and friendly interviewers conducting the assessments also seems to have an effect on increasing disclosure of information and the person's willingness to enter into subsequent alcohol treatment.

Although there were some positive experiences of medication, the qualitative literature highlights consistent fears surrounding assisted withdrawal and the unpleasant effects one may experience while in treatment. Many participants across studies fear the future and not being able to adopt appropriate coping strategies that will assist in preventing relapse once they return to their familiar social milieu. More information from staff in alcohol services may be beneficial in alleviating patient's fears about treatment.

Psychological treatment was seen to facilitate insight into one's drinking behaviour and understand the downsides of drinking. Talking with a therapist honestly and openly about alcohol helped in alleviating fears about the future and develop coping strategies. Within a residential treatment programme setting, a therapeutic ethos and a strong therapeutic relationship were regarded as the most positive aspects of alcohol treatment.

Active coping and moderation strategies, self-help groups, rehabilitation programmes and aftercare programmes were found to be helpful in preventing relapse post-treatment, and social support networks may serve as an additional motivation to change and can help promote long-term recovery. It should be noted that these findings were from studies of untreated drinkers, so this should be interpreted with caution if generalising to a population formally in treatment. Emphasis on a therapeutic relationship between healthcare practitioners and patients and good communication seem integral to promoting recovery. Social support, empathic feedback, and adequate information provision also facilitate the recovery process.

Family and friends can have an important role in supporting a person with an alcohol problem to promote and maintain change, but in order to do this they require information and support from healthcare professionals. But the strain on carers can be challenging and they may require a carer's assessment.

From a staff perspective, the qualitative studies suggest that many staff in primary care have feelings of inadequacy when delivering interventions for alcohol misuse and lack

the training they need to work confidently in this area. An improvement in staff training is required to facilitate access and engagement in treatment for people with alcohol problems. When interventions were successfully delivered, assessment and diagnostic tools were seen as crucial. In addition, thorough assessment and diagnostic tools may aid in the process of assessing and treating patients with alcohol use disorders.

Even if they were aware of a problem, many healthcare professionals felt they had inadequate training, lack of resources, or were unable to carry out motivational techniques themselves. More training about harmful drinking populations and associated interventions, as well as more awareness about how to interact with these populations from a primary care perspective, should be considered.

4.5 Qualitative analysis – people with parents who have alcohol problems

4.5.1 Introduction

As the current guideline also aims to address support needs for families/carers, the following section includes a qualitative analysis conducted using transcripts from people with parents who have alcohol problems. These were accessed from the National Association for Children of Alcoholics (NACOA) website (www.nacoa.org.uk). NACOA provides information and support to people of parents with alcohol problems (whether still in childhood or in adulthood), and the website includes personal experiences of such people in narrative form. The review team undertook their own thematic analysis of the narrative accounts to explore emergent themes that could be used to inform recommendations for the provision of care for young people of parents with alcohol problems.

4.5.2 Methods

Using all the personal experiences available from NACOA submitted from 2004 onwards, the review team analysed 46 accounts from people with parents who misuse alcohol, the large majority of whom were female. All accounts have been published on the website in their original form. The majority are written by people from the UK but there are also some from other countries, such as the US and Australia. Poems and letters were excluded from the analysis. Each transcript was read and re-read and sections of the text were collected under different headings using a qualitative software program (NVivo). Initially the text from the transcripts was divided into three broad headings that emerged from the data: impact of the parent's alcohol problems on the child's behaviour, thoughts and feelings; impact of the parent's alcohol problems on the child's psychological state/mental health; and support and services for the family and the child. Under these broad headings specific emergent themes identified separately by two researchers were extracted and regrouped under the subsections below.

4.5.3 Impact of parental alcohol problem on the child's behaviour, thoughts and feelings

Avoidance and concealing the truth

In recounting the experiences, a common theme that emerged was fear, shame and embarrassment which led to avoidance, escapism and concealing the truth about their parent with the alcohol problem. These kinds of behaviours impinged on the child's ability to enjoy simple activities, such as have a friend over to the house:

> *'I became an expert at hiding my feelings. I was scared to get a girlfriend because I was worried that she might find out. I never invited friends round to stay. I'd do anything to avoid going home… I took a job after school that involved working until 10pm and I thought that was great because I had a really good excuse not to be at home.'*

> *'As children we never invited anyone home, the embarrassment would have been too much to bear.'*

> *'I wouldn't invite even my best friend round to my house, I couldn't bear for anyone to see my father. I was worried they would talk about me, worried about what they would think of me.'*

> *'I dreaded events where parents could attend. If my dad came, he'd be drunk, sing loudly and make a fool of himself. I didn't want him there, didn't want to be different to everyone else, what child does?'*

Some people even described trying to hide the problem from themselves in order to cope:

> *'I led a double life, hiding my feelings until I'd "forgotten" I ever had any, saying I was "fine, thank you" when I was falling apart and convincing myself that it "wasn't that bad".'*

> *'I realised that I had kept all my feelings bottled inside me for so many years. So hidden that even I hadn't really noticed them.'*

Many also noted that they had no-one to talk to and very little support (see section 1.6.5), and concealing the truth made this even more difficult for others, such as teachers/friends, to recognise that there was a problem:

> *'I couldn't talk about my dad's problem or my mum's illness to anyone, my school only found out she was ill 3 months before she died, when I ran out of a lesson in tears and had to explain to a teacher.'*

> *'On the surface we were all terribly polite and we never spoke about the insanity and fear that lurked beneath the surface of our daily rituals… we were the best-mannered children in the world to strangers.'*

Others mentioned that when they tried to face the problem and discuss their worries directly with their parents, they were confronted with negative responses or abusive behaviour which prevented them from raising the issue again:

'I told her I was worried she was an alcoholic. She hit me hard across the head and shouted, you don't know what that word means. It was the last time I tried to talk to her about her drinking until I was grown up and even then I daren't do it in a direct and open way.'

'I was the first one to mention that she may have an alcohol problem, when I was 15, following an argument between my parents… the encounter led to a period of ostracizement from the family home.'

Relationships in childhood and later life

A prominent theme was the development of personal relationships and friendships in childhood and in later life. Many of the accounts reported that it was a challenge to form or maintain relationships with others. This was frequently attributed to a lack of trust:

'I struggle to form relationships with people, it is ingrained into me that nobody can be trusted, and that all promises are false. When I do form relationships with people, I cling to them tightly because I am scared they will leave me and in the end frequently this obsession only serves to push them away. I find it difficult to talk to people, and open up. I think this is something I'll never be able to do.'

'Growing up in a severely dysfunctional environment has made it so hard to fit in with other people as my reactions are so different to others and I feel very self-conscious about it. I have succeeded in getting a job at a top company…yet I don't fit in and sometimes wonder if I deserve it.'

'The effect of my childhood has caused me to not trust people (although I trust 2 good friends now)…and to pursue unsuitable relationships with men (hardly surprising after all 4 of the men in my immediate family abused me).'

Because of the struggle to form successful relationships, as well as the avoidance, many people described themselves as lonely and isolated:

'I feel negative about lots of things and have isolated myself from lots of people, know I should not be but it's so hard just now. I feel so different to other people and compare myself to my work colleagues who had a normal upbringing.'

'I became a very serious, lonely teenager who was not able to trust anyone.'

'If anyone saw her drunk I was so ashamed. As a teenager, that made me feel different and isolated. I was lonely.'

As adults, a number of people described wanting to find partners who were different from their parents, primarily people who did not have an alcohol problem. However, some did also say that they were attracted to others with similar experiences:

'Having an alcoholic father made me determined never to get myself attached to a man with any kind of habit'

'I chose my husband and father of my two children very carefully…he drank very little and had no change in personality when he did and did not obsess about where the next drink was coming from'

'I'm in a good relationship, with another child of an alcoholic who shares a lot of the same understanding.'

Triumph over adversity

People described many situations in which negative experiences and beliefs from their childhood were turned around in order to change current emotions, thoughts and behaviours into positive ones. For example, taking on different parenting skills to those of their own parents in order to be better parents, or trying to make the best of a situation:

'I vowed, even as early as eight or nine, that I would never ever inflict this kind of torture -- of being a child of an alcoholic parent -- on a child myself'

'I had hoped that having a family of my own would help to fill the emptiness inside and provide some of the love, warmth and nurturing I had missed. In bringing them up we have completely turned my parent's philosophy on its head'

'I'd come to the conclusion that I was stronger than I thought I would ever be when faced with her eventual demise...I knew I had to find something positive to do with it; to have buried the experience along with her, would have been a crime.'

'You know now that for every negative emotion there is an opposite positive...tears into laughter, fear into courage, co-dependency into mature friendship…shame into pride…lack of control into more control over your life, victim-hood into assertiveness'

'I learnt to channel my addictive tendencies into more positive things such as my great passion in life, surfing'.

High levels of responsibility

Another theme that emerged was that of increased responsibility. Some felt that they were forced to grow up quickly through practical and emotional burdens which are not usually considered the responsibility of a child:

'All my energy and time went into worrying about and saving my mother from her drunken dramas. It was extremely draining being the responsible one. I was not sleeping or eating properly, and constantly felt ill with headaches through stress.'

'I was forced into growing up too quickly and had to get on with things, doing my washing, making sure I had clean clothes for school or did my homework, getting myself a meal.'

'Without thinking about it I had denied huge parts of myself, learned to make myself invisible and to take care of myself. After all, nobody else was guaranteed to do it for me.'

High levels of responsibility were commonly reported and often led to feelings of guilt and blame, as they felt that it was partly their fault that things had gone wrong and that in retrospect they could have done more to help their parent with the alcohol problem. Some even felt that the problem was actually theirs through over-identification with their parent:

> *'I always blamed myself for all the hurt my mum caused me thinking everything was my fault'*

> *'I felt immense guilt, perhaps if I'd been to see him more often this would not have happened. Maybe I could have prevented his drinking.'*

> *'It still feels like I'm 'carrying' her problem for her, because she never admitted she had one…I understood she had a problem; she didn't and so she thought it must be my problem.'*

> *'I kind of treated her illness as my illness, as though we were both alcoholics and both had something to hide.'*

Other themes relating to impact on behaviour which were apparent but less prominent than those outlined above included: committing unlawful behaviours such as stealing; negative impacts on education and employment, such as failing exams or struggling to keep a job and experiencing a sense of relief at the death of the parent with the alcohol problem. Many also described suffering some form of abuse from family members or relations, which could have impacted on a variety of behavioural and cognitive outcomes.

4.5.4 Impact on psychological state/mental health

Fear, anxiety and worry

A theme which repeatedly appeared was that of fear, and anxiety and worry. People described feeling scared about coming home from school, worrying about bad things that may happen to their parent and generally being on edge:

> *'Coming home from school was terrifying. I knew every floorboard that creaked, every door that squeaked and became expert at moving silently. I practised when he was out.'*

> *'As a child I always knew something in my house was wrong. I had an anxious feeling most of the time and never really questioned it. I would lie awake worrying that we would get burgled and there was only me who could phone the police. My mind would go into overdrive with anxiety.'*

> *'I do still worry about my mother, I do not think a part of me will ever rest about her drinking, until the day she dies.'*

Depression and feeling low

Another theme that emerged was the experience of depression, unhappiness and despair, both during childhood and continuing into later adulthood. Some people even talked about suicidal feelings:

'I was 16 when I realised that I couldn't remember the last day that went by when I didn't cry and feel utterly miserable and unhappy. I overdosed out of depression for something to change, for someone to notice, for someone to help me.'

'I suffered low self-esteem, a lack of sense of self, self harm, an eating disorder, attempted suicide, anxiety, and depression and welcomed an abusive lover into my life.'

'I am convinced that these experiences have played a major role in allowing my life to be subsumed on occasions by misery, fear and despair.'

'You have to work at being 'happy', and fight off continually, the bogey of depression. You are constantly saddened, and unable to ignore great grief and suffering of anyone in the world, and absorb everyone's trauma like a sponge.'

'I'm suffering severe depression now and frequently think about taking my own life, have had counselling; maybe not enough of it.'

Anger

Anger was another emotion which was frequently described in the experiences, although exact reasons underlying the anger were for the most part not described:

'Forgiveness was vital for me as I had years of fear and unresolved anger. '

'I got angry with the people that looked on the bright side, 'always look on the bright side of life,' Rubbish. 'Things aren't as bad as what they seem.' Shut up. 'Things will get better, they always do.' Anger. I was confused, I did want to get better, but I didn't know how.'

'I have never ever forgiven myself for my behaviour towards her as a teenager. I'd slam doors, break things, scream, rant rave in frustration.'

Own alcohol problems

Another theme that emerged was the development of their own alcohol problems, both in adolescence and adulthood:

'Coming to terms with my mother's alcoholism took me on a rather circuitous route involving my own deep struggles with the substance, over many years. It was almost as if, despite vowing I would not end up like her, I had to experience it to understand it.'

'I was first drunk when I was 12 years old. I stayed drunk either in my head or physically, for the next 13 years it took away all the pain of being an object, OK it created so many other problems but killed the feelings when I was out my head.'

'Instead of breaking free from his restraints, I began drinking, just like he had!'

They described how they accessed help for their own drinking problems and there were mixed views about whether talking to health professionals or attending self-help groups made a difference, however the majority did report a positive outcome:

'I was in AA, and although I needed them it took years to let anyone near me. When I get that old feeling I am still the same. I still feel that for an adult child AA is a hard place to be if they do not have some kind of support behind them.'

'My girlfriend knew that I was an alcoholic and she persuaded me to enter a treatment centre…I spent 12 weeks at the centre drying out and afterwards received lots of support by joining Alcoholics Anonymous, the self-help group for recovering alcoholics. I would never have stayed sober without them but it's now been 10 years since I touched drink.'

'I started to realise that my drinking was now problem drinking and sought help from a counsellor. After talking to the counsellor, who explained the progressive nature of alcoholism, that my drinking was alcoholic and that there was only one cure: i.e. total abstention, it all fell into place.'

'I sought treatment and found nightly doses of Amitriptyline to be helpful. I have also decided to take part in a course of psychotherapy. Though I look upon the drug as a temporary measure, I will not lose sight of the principle that whatever helps me to limit the impact of the most distressing and intrusive of my experience is a good thing. I have retained control in my purposeful dealings with medical and mental health professionals.'

4.5.5 Support and services for the family and children of parents who misuse alcohol

Talking to somebody

One of the most prominent themes that emerged when discussing help and support was the need to talk to somebody about what they were feeling and thinking. Many felt this was difficult to do, but once they did manage to talk to someone they felt relieved and found it helped to discuss their problems. A few people talked specifically about how having a supportive teacher to talk to was helpful:

'The worst part was feeling alone and that I could ask no one for help. I used to dream about talking to someone and the relief that would bring but felt disloyal for even having the thought.'

'I wish I had felt that talking to someone was an option. It never even occurred to me.'

'You don't need to tell the whole world, but talking to the right people could make a big difference. This might be a good friend, a trusted teacher or an NACOA counsellor. I now realise that nobody should have to deal with these problems by themselves.'

'There is support – and although the pain, guilt and shame does come back sometimes, facing it with honesty and knowing that you are not alone, gives you the freedom to move on and build a purposeful life with meaningful relationships that help you to grow.'

'I finally realised that I needed to tell someone outside of my family, so I spoke to a teacher which helped a lot. I wish I had done that earlier. I now realise how much easier it would have been if people had known. Looking back I can see that I needed help. My teacher suggested ways in which she could help, and it sounded great, although sadly it was too late.'

Another apparent theme was how having a strong parent (who did not have a drinking problem) who tried to maintain some sort of stability at home was helpful:

'Despite all the problems alcohol caused, my Mother stood by us. She was torn apart but still put practical solutions in place.'

'My mother made enormous efforts to give us some normal family life but a lot of her attention was taken up with trying to keep my father calm and happy.'

Talking to a professional and accessing treatment

Some gained help from mental health professionals, and others tried to find out more information for themselves, for example from self-help books. Most found it helpful to talk to a professional and understand more about alcohol problems:

'Just to hear about the disease in a non-judgmental way and to be heard can end years of isolation and be profoundly healing.'

'She (doctor) was fantastic and told me that she had once watched a woman patient drink herself to death and had no intention of letting that happen again and referred me to the psychological services. That was the best thing that could have happened to me as I began to learn to cope without drinking and talk a bit about the shame that had kept me closed for so long.'

'I began to devour self-help books and trawl websites aimed at people like me…Initially just to experience the recognition was a relief. "Yes, exactly" I'd say to myself. Then I began to ask "why hasn't anyone told me this before?"'

'At college, my tutor organised counselling for me, I was really against the idea at first and went along determined not to take it seriously. But it really helped to have someone to talk to who wasn't involved in my life, who could see things from another perspective.'

'I have read all the self help books and I have to say if I hadn't read them to this day I don't think I would have ever understood why I'm like I am. Sadly it took me nearly 20 years to realise the impact it had on me. I never realised until one day I sat in a counselling session.'

However, the minority of people did mention negative experiences of accessing help:

'Three years previously I had gone to AA and found the experience profoundly disturbing. I thought of my mother over and over again, listening to very familiar stories and knew that I had to deal with my feelings about her as well and the two problems were inextricably connected.'

'Even in therapy, only the people who were there with me know what it's really like – the pain, the terror, the blood, sweat and tears, the rage of helplessness and fear'

Seeking help for the parent with an alcohol problem

Another reoccurring theme which emerged was the children and other family members trying to access help on behalf of the parent with the alcohol problem. A few people described how the family were in a situation in which they felt they needed to get the parent sectioned in order to get help:

'We were desperate at this stage and tried to convince the doctors to section her. This would have meant forcing her to have treatment in a mental health hospital. The doctor said he couldn't and with that, I think her last chance went.'

'The only thing left we could do was to try and get him sectioned. The doctors agreed and were coming round the following day for him.'

'We had her sectioned with the thought that it would make her stop and realise what she was doing to her self and the people that cared about her. But she fell off the wagon again, I called an ambulance for my mum and they had a go at me for wasting their time, my mum could have died, what was I supposed to do?!'

'We tried getting social services involved as she was physically and emotionally neglecting us all.'

'In March of this year I fought for an appointment for my father at the local rehab clinic and took him myself. He was admitted and diagnosed with Wernicke's Syndrome.'

Others discussed trying to persuade their parent to access some form of help, but the majority reported an unsuccessful outcome:

'I have tried every trick in the book to get my dad to go and get help. But right now, it seems I am at a dead end'

'The subject of my mothers drinking is occasionally mentioned around my mother but her reply is she knows she needs help. She never seeks it.'

4.5.6 Summary of thematic analysis

There are some overarching themes experienced in childhood by people with parents who misuse alcohol. A dominant theme was that of avoidance and hiding the truth, which stemmed primarily from shame, fear and wanting a sense of normality. Concealing feelings and thoughts made approaching other people or services for support difficult, when most people just wanted to talk to somebody. This may have been exacerbated by feelings of anxiety and worry, in addition to a sense of guilt, self-blame and heightened responsibility towards the parent. When they did seek help on behalf of their parent, it seemed to occur in quite desperate circumstances, such as getting their parent sectioned. This suggests that children of parents who misuse alcohol do not, or cannot, access the services and support they need easily.

There were also overarching themes experienced in adulthood which seemed to originate from childhood experience. Many people struggled to form stable relationships which was often put down to lack of trust and self-isolation, which impacted on work, social life and the ability to maintain a successful relationship with a partner. Such problems could have originated from not being able to form 'normal' friendships in childhood. Depression, and to some extent anxiety, emerged as longstanding psychological problems attributed to various childhood experiences as well as personal traits such as low self-esteem. Development of own drinking problem was also a theme, in which alcohol was used to block out negative thoughts and experiences, or even used in an attempt to identify with the parent. There were also a range of common life choices which emerged, predominantly an impact on relationship choices and parenting skills. Some people also reported overcoming adversity by transferring the negative behaviours, thoughts and feelings into the positive ones.

There are some limitations to the qualitative analysis for this guideline. As the review team relied only on transcripts submitted to NACOA, information on other issues that could be particularly pertinent for children with parents who misuse alcohol may not have been identified. Moreover, people who have visited the NACOA website to submit their accounts may over-represent a help-seeking population. Finally, while some accounts are based on experiences which occurred recently, others occurred a long time ago; therefore there may be differences in attitudes, information and services available.

4.6 From evidence to recommendations

This section is a combined summary of the themes from the qualitative analysis and the literature review. It should be noted that the populations from the two sections differ: the qualitative analysis looked at the experiences in childhood of people with parents who misused alcohol, whereas the narrative summary of the qualitative literature looked at people who themselves had with current or previous alcohol problems.

4.6.1 Understanding alcohol problems

Many of the studies identified a cycle of alcohol misuse and highlighted the process towards abstinence. The person's social milieu was frequently cited as encouraging the person to drink more, and also served as powerful triggers once a person has decided

to stop drinking. And yet social networks can also be a powerful influence in promoting and maintaining positive change. Furthermore, strategies for moderating drinking and becoming abstinent, as well as reasons for stopping drinking, are important in contributing to our understanding of alcohol dependence and misuse, and how staff can better identify and help maintain positive change.

4.6.2 Access and barriers to treatment

Stigma was discussed in the qualitative analysis as well as in the literature review. Children of parents who have alcohol problems often concealed their feelings and thoughts, which was a barrier to getting help or support. In the literature review, stigma was experienced both externally (mostly from healthcare professionals) and internally; internal stigma could result in concealment of the person's alcohol problem from others due to fear or shame.

Women felt additional internal stigma due to alcohol misuse being perceived largely as a male problem. Positive interactions with healthcare practitioners involved an empathic, non-judgemental approach employed, but there were also negative interactions stemming from feeling uncomfortable when discussing alcohol problems, a lack of childcare opportunities, and rigid treatment programmes that did not allow for flexible timing where one could simultaneously enter treatment and care for their family.

In the qualitative analysis of experience in childhood by people with parents who misuse alcohol, a dominant theme was avoidance and hiding the truth; this concealment of feelings led to barriers in accessing services or seeking out help or support. This suggests that children of parents who misuse alcohol do not, or cannot, access the services and support they need easily. More opportunities to support those who have parents with alcohol problems, as well as finding ways for them to talk about their emotions, would be beneficial and may help prevent the child or young person developing their own alcohol problems later in life. Furthermore, and echoing the review of the qualitative literature, many children struggled to form stable relationships, which, once again, underscores the importance of building positive support networks.

4.6.3 Experience of treatment

Providing an assessment to a person seeking treatment for alcohol problems was perceived as extremely beneficial in terms of increasing awareness of their own drinking and giving them an opportunity to discuss their problems. The therapeutic relationship between the interviewee and interviewer was judged to be highly important and as a result, a well-conducted, motivational assessment seems both useful and necessary in increasing motivation to change and engagement in treatment.

The most commonly cited emotion regarding assisted withdrawal was fear about the treatment process, the medication and about coping without alcohol. The two studies highlighted that more information could be provided prior to treatment to prepare a person for assisted withdrawal, that more could be done to help service users transfer from the treatment programme to the community, and that there should be a greater emphasis on coping skills and relapse prevention in the post-treatment period.

The positive aspects and benefits of a therapeutic relationship both in a treatment setting and in assessment procedures were cited frequently. This highlights the need for healthcare practitioners to approach those with alcohol problems in an encouraging and non-judgemental manner.

4.6.4 Experience of family members and carers

Given the challenges of caring for someone with an alcohol problem, which is revealed by both the literature review and the qualitative analysis, more information and support should be available to carers, and there should be an emphasis on including them in the treatment process, if this is appropriate and the service user agrees. Furthermore, with the understanding of how important positive social support networks are in maintaining positive change, helping carers supporting their supportive role is crucial in order to promote change. Children of parents who have alcohol problems will have specific needs that should be recognised as described above.

4.6.5 Experience of recovery

One significant theme that emerged from the studies was the importance of experiencing a turning point in one's life, which serves as a motivation to stop drinking. After this turning point many people with alcohol problems used active coping and moderation strategies in order to limit or stop alcohol consumption, and a number of the studies touch on the importance of positive social support networks and self-help groups. Should be noted this was in untreated drinkers (4 out of 5 studies) so this should be interpreted with caution if generalising to a population formally in treatment, although the one other study lends support to the untreated accounts.

4.6.6 Staff experiences

The staff perspective highlighted the difficulty of approaching people with alcohol problems due to the often sensitive nature of the topic of alcohol. Many healthcare professionals found it difficult to screen for alcohol misuse and implement brief interventions, and felt that more training would be beneficial around delivering treatments as well as structuring communication about alcohol in routine care. Effective diagnostic tools that allowed staff to employ an indirect, non-confrontational approach were deemed to be helpful.

4.6.7 Recommendations

Building a trusting relationship and providing information

4.6.7.1 When working with people who misuse alcohol:

- build a trusting relationship and work in a supportive, empathic and non-judgmental manner
- take into account that stigma and discrimination is often associated with alcohol misuse and that minimising the problem may be part of the service user's presentation

- make sure that discussions take place in settings in which confidentiality, privacy and dignity are respected.

4.6.7.2 When working with people who misuse alcohol:

- provide information appropriate to their level of understanding about the nature and treatment of alcohol misuse
- avoid clinical language without explanation
- ensure that comprehensive written information is available in the appropriate language or, for those who cannot use written text, in an accessible format
- provide and work effectively with independent interpreters (that is, someone who is not known to the service user) if needed.

Working with and supporting families and carers

4.6.7.3 Encourage families and carers to be involved in the treatment and care of people who misuse alcohol to help support and maintain positive change.

4.6.7.4 When families and carers are involved in supporting a person who misuses alcohol, discuss concerns about the impact of alcohol misuse on themselves and other family members, and:

- provide written and verbal information on alcohol misuse and its management, including how families or carers can support the service user
- offer a carer's assessment of their caring, physical and mental health needs where necessary
- negotiate with the service user and their family or carer about the family or carer's involvement in their care and the sharing of information; pay proper attention to the service user's right to confidentiality.

4.6.7.5 All staff in contact with parents who misuse alcohol and who have care of or regular contact with their children, should:

- take account of the impact of the parent's drinking on the child's social network, education, mental health and own alcohol use
- be aware of and comply with the requirements of the Children Act (2004).

5. The organisation and delivery of care for people who misuse alcohol

Section 1 – Introduction to the organisation and delivery of care

5.1 Introduction

The chapter provides an overview of the types of services available for people who misuse alcohol and how they are currently organised, and reviews the evidence to guide future development and improvements in service provision for alcohol misusers. The key concepts underpinning service organisation and delivery will be explained and their nature and role will be defined. These concepts will build on existing guidance in the field, notably *Models of Care for Alcohol Misusers* developed by the National Treatment Agency (MoCAM; DH, 2006a) and the *Review of the Effectiveness of Treatment for Alcohol Problems* (Raistrick *et al*., 2006). Where relevant parallel guidance from NICE on alcohol services will be referred to, in particular the NICE guideline on prevention and early detection (NICE 2010a) and the NICE guideline on management of alcohol-related physical complications (NICE, 2010b). As this guideline was the last in the suite of NICE guidelines on alcohol misuse to be developed, this chapter aims to integrate and provide an overview of how the various guidelines are related in order to support the development of a comprehensive pathway for the care and treatment of alcohol misuse.

In Chapter 2 it was highlighted that alcohol service commissioning and provision across England is variable and in some cases poorly integrated (NAO, 2008). Hence the availability of alcohol services and the extent to which it meets the needs of alcohol misusers varies across England (Drummond *et al*., 2005). The Guideline Development Group also took the view that there is a lack of clarity in the field about which kinds of alcohol services are most beneficial for which people. For example who should be treated in a community setting compared to a residential setting, what constitutes an adequate assessment of individual's presenting needs and how an individual's care can be most appropriately coordinated are all key questions that need to be addressed. This lack of clarity has resulted in diverse commissioning and provision of alcohol services.

This chapter will also highlight that the provision of care for alcohol misusers is not solely the responsibility of agencies and staff who specialise in alcohol treatment. Staff across a wide range of health, social care and criminal justice services, who are not exclusively working with alcohol misusers, but regularly come into contact with them in the course of providing other services, also have a crucial role to play in helping people to access appropriate care. In some cases staff that are not alcohol treatment specialists (most notably those working in primary care) will have a role in delivering key elements of an integrated care pathway for this population.

The chapter begins by describing the organising principles of care for alcohol misusers, followed by a description of the different types of services, and how they are currently organised; where relevant, existing definitions and frameworks will be referred to. We will then review the principles and methods of care delivery, including assessment, care coordination, integrated care pathways and stepped care. We will review evidence on case management, stepped care, and assertive community treatment, assessment, assisted alcohol withdrawal, and care delivered in residential versus community settings. The chapter will conclude with a description of the main care pathways stemming from the findings of the evidence review.

5.2 Organising principles of care

In the introductory chapter we highlighted the diverse range and severity of alcohol misuse which exist in the general population. These range from hazardous and harmful drinkers through to people with alcohol dependence of varying degrees of severity. Alcohol misuse is associated with a wide range of physical, psychological and social problems, some of which are a consequence of drinking and others are incidental, but often highly relevant, in planning and delivering individual care. For example, a harmful alcohol user who is homeless and suffering from mental health problems may have more significant care needs than a more severely dependent drinker who has stable accommodation and employment and no psychiatric comorbidity.

It was also noted in the Chapter 2 that in many cases alcohol misuse remits without any form of formal intervention or contact with the health or social care system, let alone specialist alcohol treatment. Studies of what has been referred to as 'spontaneous remission' from alcohol misuse find that this is often attributed, by individuals, to both positive and negative life events, such as getting married, taking on child care responsibilities, or experiencing a negative consequence of drinking such as being arrested, having an accident or experiencing alcoholic hepatitis. It therefore follows that not everyone in the general population who meets the criteria for a diagnosis of an alcohol misuse requires specialist treatment. Often a brief intervention from a GP, for example, may be sufficient to help an individual reduce their drinking to a less harmful level (see NICE guideline on prevention and early detection (NICE 2010a).

Nevertheless, the level of alcohol consumption, and the severity of alcohol dependence and alcohol related problems are positively correlated such that people with more severe alcohol dependence usually have more severe problems and greater care needs (Wu & Ringwalt, 2004). Also, a proportion of people will require professional intervention to achieve sufficient change in their drinking behaviour, or to shorten the course of their alcohol use disorder.

A useful framework for this spectrum of need and the intensity of professional responses was provided by Raistrick and colleagues (2006), adapted from work originally developed the U.S. Institute of Medicine (2003) (Figure 1). Whilst they noted that alcohol problems exist on a continuum of severity, rather than in categories, and that an individual can move between categories over time, the framework provides a useful general principle that people with more severe problems generally require more intensive and specialised interventions. While matching alcohol misusers to different treatment intensities based on the severity of their problems has some empirical

support (Mattson *et al.*, 1994) this has not generally been borne out in studies designed specifically to test matching hypotheses (Drummond, 2009). This issue will be explored in more detail throughout this guideline.

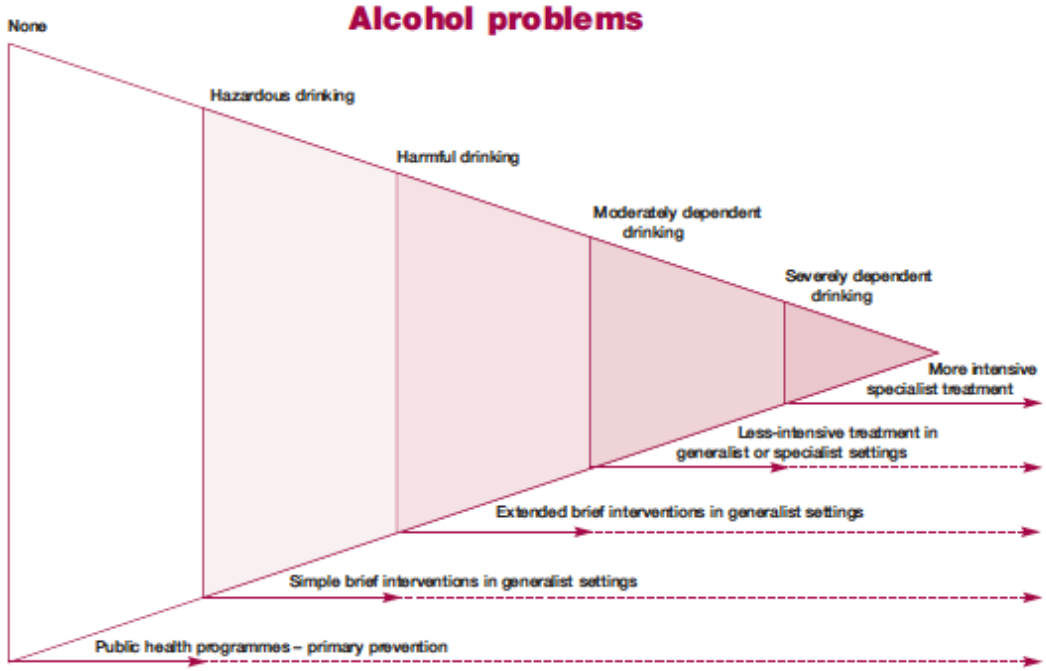


Figure 3: A spectrum of responses to alcohol problems Reproduced from a review of the effectiveness of treatment for alcohol problems (Raistrick *et al.*, 2006).

The triangle shown in figure 1 is a schematic representation of the population of England, with the spectrum of alcohol problems experienced by the population and their relative prevalence shown along the upper side of the figure. Responses to these problems are shown along the lower side. The dotted lines suggest that primary prevention, simple brief intervention, extended brief intervention and less-intensive treatment may have effects beyond their main target area. Although the figure is not drawn to scale, the prevalence in the population of each of the categories of alcohol problem is approximated by the area of the triangle occupied; most people have no alcohol problems, a very large number show risky consumption but no current problems, many have risky consumption and less serious alcohol problems, some have moderate dependence and problems and a few have severe dependence or complicated alcohol problems.

5.3 Services for people who misuse alcohol

5.3.1 Introduction

The provision of alcohol services in England from the Second World War until around the 1970s, was driven by a view of alcoholism as an all or nothing disease state affecting a relatively small proportion of the population, and requiring intensive, specialist treatment with the goal of complete abstinence from alcohol, often provided in inpatient specialist units closely affiliated with the Alcoholics Anonymous fellowship (Drummond, 2009). From the 1970s there came greater recognition of a

wider spectrum of alcohol problems which could respond to less intensive interventions, and the development of pubic health approaches to alcohol misuse. This, combined with evidence from randomised trials which questioned the value of inpatient treatment, led to a shift towards more community based care and early brief interventions provided by general practitioners. Many of the large regional inpatient alcohol units in England closed and many of the NHS staff moved to work in newly created community alcohol teams, along with growth in community based non-statutory alcohol counselling services. The current service provision in England with its patchwork of brief alcohol interventions provided by GPs, NHS and non-statutory specialist community alcohol services, some remaining NHS inpatient units providing mainly assisted alcohol withdrawal, and a declining number of residential alcohol rehabilitation agencies, mostly in the non-statutory or private sectors, are a legacy of this gradual and incomplete shift towards community based care.

5.3.2 Classification of interventions and services

Services and interventions for alcohol misuse can be classified in several different ways. *Models of Care in the Treatment of Adult Drug Misusers* (NTA, 2002; 2006b) and MoCAM (DH, 2006a) describes individual interventions as belonging to different Tiers, within a 4 Tier framework. As noted in MoCAM this has been widely interpreted in the field as individual *agencies* rather than *interventions* belonging to Tiers which have had unintended consequences. Interventions are individual elements of care (for example, a brief intervention, assisted alcohol withdrawal or cognitive behaviour therapy) which, when combined, comprise a programme of care for an individual alcohol misuser. These interventions can, and often are, delivered by a range of both generic (for example, GPs, physicians in acute hospitals, prison healthcare staff) and alcohol specialist staff working in a wide range of agencies (for example, NHS, non-statutory, criminal justice, and social care). So the Tier to which an intervention belongs is determined by its nature and intensity, rather than the agency delivering it.

5.3.3 Alcohol interventions

Within MoCAM *Tier 1 interventions* include: identification of alcohol misuse; provision of information on sensible drinking; simple brief interventions to reduce alcohol related harm; and referral of those with alcohol dependence or harm for more intensive interventions. These can be delivered by a wide range of staff in a various settings, including accident and emergency departments, primary care, acute hospitals, mental health services, criminal justice services and social services.

Tier 2 interventions include open access facilities and outreach that provide: alcohol-specific advice, information and support; extended brief interventions; and triage assessment and referral of those with more serious alcohol-related problems for "care planned" treatment. "Care planned" treatment refers to the process of planning and reviewing care within the context of structured alcohol treatment, and this is located within Tier 3. If staff have the appropriate competencies to deliver Tier 2 interventions, these can be delivered by the same range of agencies as Tier 1 interventions.

Tier 3 interventions include provision of community based specialist alcohol misuse assessment, and alcohol treatment that is coordinated and planned (see below). These

include comprehensive assessment, structured psychological interventions or pharmacological interventions which aim to prevent relapse, community-based assisted alcohol withdrawal, day programmes and specialist alcohol liaison provided to for example, acute hospitals by specialist staff. Tier 3 interventions are usually provided by staff working in specialist alcohol treatment agencies both NHS and non-statutory (although the latter are often funded by the NHS to provide these interventions). Important exceptions to this are GPs who may provide more specialised interventions within a Direct Enhanced Services contract (NHS Employers, 2008). Interventions provided by GPs often involve assisted alcohol withdrawal in the community or prescribing of medication for relapse prevention. As with interventions in other tiers, staff need to have the relevant competence to be able to provide them safely and effectively.

Tier 4 interventions include the provision of residential, specialised alcohol treatments which are planned and coordinated to ensure continuity of care and aftercare. These interventions include comprehensive assessment, inpatient assisted alcohol withdrawal and structured psychosocial interventions provided in a residential setting, including residential rehabilitation. Tier 4 interventions are usually provided by specialist alcohol inpatient or residential rehabilitation units. However, assisted alcohol withdrawal is often provided in other residential settings, including acute hospitals, mental health inpatient services, police custody, and prisons, delivered by medical and other staff whose primary role is not specialist alcohol treatment.

5.3.4 Agencies

A diverse range of health, social care and criminal justice agencies provide alcohol interventions. These agencies can be classified into specialist alcohol treatment agencies, whose primary role it is to provide interventions for alcohol misusers, and generic agencies, which are not primarily focused on alcohol treatment (NTA, 2006). In practice the majority of specialist alcohol agencies also provide treatment for drug misusers. Specialist alcohol treatment agencies are provided by NHS trusts (usually mental health NHS trusts), non-statutory agencies and the private sector, with considerable overlap in the range of interventions provided across the different sectors. However, many of these agencies are funded by the NHS. Some agencies provide both community based and residential interventions, whereas others primarily deliver interventions in one setting. For example, specialist NHS alcohol treatment services often have a community alcohol (or drug and alcohol) team linked to a specialist inpatient alcohol treatment unit in the same locality, with some staff working in both settings. Some non-statutory agencies exclusively provide residential rehabilitation with a regional or national catchment area, or community based day programmes with a smaller local catchment area. There is considerable diversity in the nature of provision across agencies and different parts of the country, in part reflecting differences in commissioning patterns (Drummond *et al*., 2005)

A national survey of alcohol treatment agencies in England, conducted in 2005 as part of the Alcohol Needs Assessment project (Drummond *et al*., 2005), identified 696 agencies providing specialist alcohol interventions. Nearly 69% of alcohol agencies were community based, and 31% were residential services. One third were primarily alcohol services and 58% were combined drug and alcohol services. Over half of all agencies were non-statutory, one third statutory (NHS) and 8% private sector.

Interventions provided by these agencies were classified according to MoCAM criteria. Community agencies most commonly provided advice, brief interventions and structured psychological interventions. Residential agencies most commonly provided residential rehabilitation and inpatient treatment, including assisted withdrawal. Overall, 45% of community agencies and 46% of residential agencies provided assisted alcohol withdrawal. Residential agencies reported greater severity of alcohol problems in their client group, with 91% of clients said to be alcohol dependent compared with 71% of community agency clients (Drummond *et al.*, 2005). The estimated annual spend on specialist alcohol treatment in England was £217M and the estimated number of whole time equivalent staff working in this sector was 4,250 (Drummond *et al.*, 2005).

The American Society of Addiction Medicine (ASAM) has developed criteria to define different types of services, some of which are partly relevant to the UK. Some aspects of their classification are helpful in understanding the terminology used later in this chapter in the evidence review and the GDG recommendations.

ASAM defines 4 levels of care (ASAM, 2001)(see Box 1). Level I outpatient treatment involves regular scheduled sessions at a specialist treatment centre, whereas Level II refers to more intensive outpatient treatment/partial hospitalisation. Both fit within Tier 3 community based interventions in the MoCAM framework, but they offer a different intensity of intervention. Level II is closest to what has been described in England as an intensive day programme, although the typical programme in England does not offer a 7-days per week service. The Level I care is the more typical provision in England.

ASAM Levels III and IV both fit within MoCAM Tier 4 interventions. Level III is residential (medically monitored) treatment which is closest to residential rehabilitation in England and provides medical cover, often by local GPs who are not necessarily specialists in alcohol treatment. Level IV is medically managed intensive inpatient treatment which is closest to NHS provided inpatient treatment in England.

Box 2. Levels of care (American Society of Addiction Medicine, 2001)

Level I – Outpatient treatment
Treatment provided in regularly scheduled sessions at a treatment centre, designed to help the individual achieve changes in their alcohol use and physical, psychological and social functioning

Level II – Intensive outpatient treatment/partial hospitalisation
An organised outpatient service that delivers treatment services during the day, before or after work or school, in the evenings or on weekends. Such treatment may include medical and psychiatric assessment and treatment, medication, psychological interventions, and educational, housing and employment support.

Level III – Residential (medically-monitored) treatment
Organised services staffed by designated addiction treatment and mental health personnel who provide a planned regimen of care in a 24-hour live-in setting. Such services adhere to defined sets of policies and procedures. They are housed in, or affiliated with, permanent facilities where patients can reside safely. They are staffed

24 hours a day. They all serve individuals who need safe and stable living environments in order to develop their recovery skills. Such living environments may be housed in the same facility where treatment services are provided or they may be in a separate facility affiliated with the treatment provider

Level IV – Medically managed intensive inpatient treatment
Provide a planned regimen of 24-hour medically directed evaluation, care and treatment of mental and substance-related disorders in an acute care inpatient setting. They are staffed by designated addiction specialist doctors, including psychiatrists, as well as other mental-health and specialist addiction clinicians. Such services are delivered under a defined set of policies and procedures and have permanent facilities that include inpatient beds. They provide care to patients whose mental and substance-related problems are so severe that they require primary biomedical, psychiatric and nursing care. Treatment is provided 24 hours a day, and the full resources of a general acute care hospital or psychiatric hospital are available. The treatment is specific to mental and substance-related disorders – however, the skills of the interdisciplinary team and the availability of support services allow the conjoint treatment of any co-occurring biomedical conditions that need to be addressed.

In England, generic agencies providing interventions for alcohol misusers are also diverse. Important amongst these are general NHS services and criminal justice agencies. Within the NHS, GPs frequently come into contact with alcohol misusers and have an important role to play in providing Tier 1 interventions, including early identification, advice, brief intervention and referral of patients to specialist alcohol agencies. Some primary care based staff, including GPs, practice nurses and counsellors, also provide more complex alcohol interventions including assisted alcohol withdrawal, and psychological and pharmacological interventions. Sometimes this is provided in a collaborative shared care arrangement with a specialist alcohol treatment agency. Some GPs also provide medical support to residential non-statutory agencies such as assisted alcohol withdrawal.

In relation to the criminal justice system, forensic medical examiners are often called upon to provide assessment and management of detainees in police custody who are alcohol misusers. This often includes the management of acute conditions, such as severe alcohol intoxication or alcohol withdrawal. Prison health services also have a key role in the assessment and management of prisoners who are alcohol misusers, including assessment and management of assisted alcohol withdrawal.

In acute hospitals a wide range of health professionals come into contact with alcohol misusers. In particular, staff in accident and emergency (A&E) departments often encounter patients with alcohol related presentations, such as accidents and injuries sustained whilst intoxicated with alcohol, and can play an important role in early identification and intervention. Alcohol misusing patients admitted to acute hospitals, either in an emergency or for elective treatment, present an opportunity for early identification and intervention. Some acute hospitals will have specialist alcohol liaison teams who support the acute care staff and provide assessment, intervention and referral to specialist alcohol agencies. A&E staff also encounter patients presenting

in acute unplanned alcohol withdrawal (NICE, 2010b) and some of these patients will require assisted alcohol withdrawal.

Alcohol misuse is common in clients attending mental health services, particularly among the severely mentally ill (Weaver *et al.*, 2003) but seldom identified by mental health staff (Barnaby *et al.*, 2003). This represents an important missed opportunity to provide early alcohol intervention or referral to specialist services. Also mental health clients attending both inpatient and community mental health services will often require assisted alcohol withdrawal. So staff working in these generic settings need to be competent to identify, assess and manage the complications of alcohol misuse.

5.3.5 Coordination and organisation of care

From the foregoing it is apparent that the range of interventions, and the agencies that provide them, are highly complex and diverse, with considerable geographic variation. This diversity presents challenges both for the individual alcohol misuser and at a treatment system level. For the alcohol misuser entering treatment for the first time, the array of interventions, agencies and staff can be bewildering. Clients, therefore, need considerable help in orientation and understanding what is available to them and what services they might require. Also, the alcohol interventions an individual requires may be provided by several different agencies in the course of an episode of care, as well as needing care from a range of generic agencies for physical, psychological or social problems. As clients move between different agencies there is considerable potential for premature disengagement. There is therefore the care of an individual client needs to be planned and coordinated.

5.3.6 Case coordination

Several terms have been used to describe the coordination of care within specialist alcohol services, including case management, keyworking, care coordination, care planning, and assertive outreach. In MoCAM (DH, 2006) there is an expectation that all cases would be case coordinated. These include harmful drinkers who respond to a brief intervention do not usually require more intensive form of case coordination such as case management. More severely dependent drinkers with complex mental or physical comorbidities or social needs usually require considerable case management due to the complex nature of their problems and/or the wide range of agencies involved. Some studies reviewed in this chapter include more assertive approaches in supporting clients, including 'Assertive Community Treatment'. '

Case management, as defined in this guideline, has several elements. The individual case manager is responsible for assessment of the individual client's needs, development of a care plan in collaboration with the client and relevant others (including relatives and carers, other staff in specialist and generic agencies involved in the client's care), coordination of the delivery of interventions and services, providing support to the client to assist in access to and engagement with services and interventions. The case manager will use psychological interventions such as motivational interviewing to enhance the client's readiness to engage with treatment. The case manager is also responsible for monitoring the outcome of interventions and revising the care plan accordingly. Case management is a skilled task which requires appropriately competent staff to deliver it effectively. Further, to discharge this function effectively, case managers need to limit the number of clients they can

support at any one time. Case management is a Tier 3/4 intervention within MoCAM and should begin with a comprehensive specialist assessment.

5.3.7 Integrated care pathways and stepped care

An integrated care pathway (ICP) "describes the nature and anticipated course of treatment for a particular client and a predetermined plan of treatment" (NTA, 2006). ICPs have a function at both an individual and a treatment system level. At the individual level the care plan should describe the client's personalised care pathway, designed to meet the assessed needs, the planned interventions, and the agencies and staff intended to deliver them. The pathway needs to be integrated in that it shows a logical progression of steps with interventions being provided at the appropriate stages. For example an alcohol dependent client may initially require inpatient assisted alcohol withdrawal followed by a structured psychosocial intervention in an alcohol day programme, followed by specialised psychotherapy for post traumatic stress disorder, followed by vocational services to support a return to work. Each of these elements of care may be delivered by different agencies in different locations, and the pathway needs to be integrated to deliver maximum benefit and minimise the client's premature disengagement.

Stepped care is a method of organising and providing services in the most cost efficient way to meet individual needs (Sobell & Sobell, 2000). Two defining characteristics are common to all stepped care systems (Davison, 2000). The first concerns the provision of the least restrictive and least costly intervention (including assessments) that will be effective for an individual's presenting problems, and the second is concerned with building in a self-correcting mechanism. Escalating levels of response to the complexity or severity of the disorder are often implicit in the organisation and delivery of many healthcare interventions, but a stepped care system is an explicit attempt to formalise the delivery and monitoring of patient flows through the system. In establishing a stepped care approach, consideration should not only be given to the degree of restrictiveness associated with a treatment, and its costs and effectiveness, but also the likelihood of its uptake by a patient and the likely impact that an unsuccessful intervention will have on the probability of other interventions being taken up.

Within this approach alcohol misusers are initially offered the least intensive intervention that is acceptable and most likely to be effective for them, followed by increasingly intensive interventions for those not responding to the less intensive interventions. A stepped care algorithm effectively describes an integrated care pathway which accommodates individual needs and responses to interventions (Drummond *et al*., 2009). This approach has gained increasing currency in other mental health disorders, including depression (NICE, 2009). Stepped care approach has also been supported by recent guidance from the National Treatment Agency and the Department of Health (NTA, 2006; Raistrick *et al*., 2006). The evidence for stepped care for alcohol misusers is reviewed later in this chapter.

5.3.8 Relationship of this guidance to other NICE guidelines

This guideline is focused on the identification, assessment and management of harmful alcohol use and alcohol dependence (alcohol misuse). The NICE guideline on

prevention and early detection (NICE 2010a) is concerned with a range of preventive strategies for alcohol use disorders. This includes screening for alcohol misuse and brief intervention which is not only a Tier 1 alcohol intervention but also potentially acts as a gateway to other, more intensive interventions for alcohol misusers. The NICE guideline on management of alcohol-related physical complications (NICE, 2010b) is focused on the management of a wide range of physical consequences of alcohol misuse. These include the management of assisted alcohol withdrawal in acute hospital settings, which are Tier 4 interventions. However, the guideline is restricted to the management of unplanned assisted alcohol withdrawal, i.e. in circumstances where a patient presents to hospital already in a state of alcohol withdrawal. This guideline is concerned with a much wider range of potential scenarios where alcohol misusers may require assisted alcohol withdrawal, including where assisted withdrawal is provided in a planned way as part of an integrated programme of alcohol specialist care, and where alcohol misusers are identified as being at risk of developing alcohol withdrawal in acute hospitals or prison settings and therefore require planned assisted alcohol withdrawal.

Section 2 – Evaluating the organisation of care for people who misuse alcohol

5.4 Clinical question

In adults with alcohol misuse, what is the clinical efficacy, cost-effectiveness, and safety of, and patient satisfaction associated with different systems for the organisation of care?

5.5 Introduction

This section presents reviews of the evidence for case management, assertive community treatment and stepped care. The reviews and evidence summaries are presented separately, but a combined section on evidence into recommendation is presented at the end of this section, along with the recommendations developed by the GDG. In reviewing the evidence for the effectiveness of different service delivery models, the GDG initially decided to focus on RCTs. The use of this type of study design to evaluate service-level interventions gives rise to a number of problems, including the definition of the interventions and the specification of the comparator and interpreting results of trials of complex healthcare interventions across different healthcare systems (Campbell *et al*., 2004). As demonstrated in the section below, the use of RCTs was further complicated by the limited number of studies identified. This led to the GDG to include a range of observational studies in a review of the service delivery models, both to increase the available evidence base and also because some observational studies may provide richer data on what services do, how they do it, and how they differ from alternative types of service and the standard care they hope to replace. Given the nature of the studies identified, a narrative synthesis of observational and RCT studies that were relevant to the intervention, but could not be meta-analysed was conducted after the review of RCTs.

5.6 Case management

5.6.1 Introduction

For the purposes of the guideline, case management is defined as the bringing together of the assessment, planning, coordination and monitoring of care under one umbrella. In a number of cases, all these four activities will be undertaken by one individual, but in other cases, some of the above functions will be undertaken by other team members or health professionals but coordinated by one individual. In some case management interventions the case manager adopts largely a brokerage role, in other cases the case manager takes on an active and direct clinical role. Where the case manager takes on an active clinical role using a specific intervention (for example, CBT) such interventions were excluded from the case management review and included in another relevant review within this guideline. Case management may also vary in its duration and intensity. For the purposes of this guideline, the GDG took the view that

the intervention should be of sufficient duration to allow for all four functions to be undertaken.

5.6.2 Clinical review protocol

Information about the databases searched and the inclusion/exclusion criteria used for this section of the guideline can be found in Table 1.

Table 6. Databases searched and inclusion/exclusion criteria for clinical evidence.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs, Systematic Reviews
Patient population	People with alcohol dependence or harmful alcohol use
Interventions	Case management vs. Other Treatment Case management vs. Treatment as Usual
Outcomes	Aftercare attendance; engagement in aftercare; abstinence; drinking frequency measures (for example, number of days drinking in the past month); quantity of alcohol consumption measures (for example, drinks per drinking day); number retained in treatment; relapse; lapse

5.6.3 Studies considered[6]

The review team conducted a new systematic search for RCTs and systematic reviews that assessed the benefits and downsides of case management and related health economic evidence.

Five trials (three RCTs, two observational studies) relating to clinical evidence met the eligibility criteria set by the GDG, providing data on 1261 participants. Of these, all five were published in peer-reviewed journals between 1983 and 1999. In addition, 13 studies were excluded from the analysis. The most common reason for exclusion was no usable outcome data, or the intervention was aimed at a primarily drug misusing population, rather than alcohol misuse. Summary study characteristics of the included studies are presented in Table 2 (further information about both included and excluded studies can be found in Appendix 16b).

Case management versus treatment as usual

There were three RCTs and two observational studies involving comparisons of case management and treatment as usual (AHLES1983, COX1998, CONRAD1998, PATTERSON1997, MCLELLAN1999). AHLES1983 compared case management with treatment as usual (standard aftercare arrangements), where the importance of attending aftercare was emphasised but not enforced. Patients were scheduled for one aftercare session at discharge, and aftercare consisted of individual problem oriented counselling. COX1998 compared case management with treatment as usual (there was no further description of treatment as usual). CONRAD1998 compared two types of residential inpatient care, with the experimental group being case managed, whereas

[6] Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

the control group participated in the residential care programme without case management.

For the purposes of this guideline, two observational were also included in the review. PATTERSON1997 compared the addition of a community psychiatric nurse (CPN) to aftercare versus standard hospital care. Standard hospital care consisted of an offer of review appointments every 6 weeks following discharge, and provided with hospital contact information Lastly, MCLELLAN1999 compared case management versus treatment as usual (no case management). In the standard care condition, participants received group abstinence-oriented outpatient drug abuse counselling twice weekly. In the case management condition, participants received a clinical case manager to provide support for housing, medical care, legal advice and parenting classes, in addition to the drug counselling programme. For a graphical representation of the data, these two studies were inputted into the forest plot to compare with the results of the RCTs, however it should be noted that the outcomes and data were not pooled with the data found in the RCTs.

Table 7: Study information table for trials of case management

	Case management versus treatment as usual
Total no. of trials (total no. of participants)	5 (N =1261)
Study ID	AHLES1983 COX1998 CONRAD1998 MCLELLAN1999 (observational) PATTERSON1997 (observational)
Baseline severity: mean (SD)	AHLES1983: 80% admitted to levels of drinking within the abusive range COX1998: Days of drinking (any alcohol use) in last 30 days: CM: 23.6(9.2) Control: 23 8(9.1) CONRAD1998: Days of alcohol use in past 30 days (mean): 18.4 for control group, 19.0 for experimental group MCLELLAN1999: Whole sample on average reported 13.4 years of problem alcohol use (12.1) PATTERSON1997: Daily alcohol (units) (m, SD) CPN aftercare: 39.4(18.3) Standard aftercare: 42.9(16.6)
Length of follow-up	AHLES1983: 6- and 12-month COX1998: Assessed in 6 month intervals up to 2–year follow-up CONRAD1998: 3, 6, 9 months during enrolment and 12, 18, and 24 months after completion of treatment. MCLELLAN1999: 6 month PATTERSON1997: Assessed at 1,2,3,4,5 year post-treatment

5.6.4 Clinical evidence for case management

Evidence from the important outcomes and overall quality of evidence are presented in T
Table 7 and Table 8. The associated forest plots can be found in Appendix 17a.

Table 8: Case management versus treatment as usual

Outcome or Subgroup	*k*	Total N	Stats	Effect (95% CI)	Quality of the evidenc (GRADE)
1. Lapse (non-abstinence)			RR[M-H, Random, 95% CI]		
1.1. At 6-month follow-up	1	36	RR[M-H, Random, 95% CI]	0.27 (0.11,0.65)	⊕⊕⊕O MODERATE
1.2. At 12-month follow-up (RCT)	1	36	RR[M-H, Random, 95% CI]	0.75 (0.52,1.08)	⊕⊕⊕O MODERATE
1.3. At 2-year follow-up (non-RCT)	1	122	RR[M-H, Random, 95% CI]	0.88 (0.69,1.12)	⊕OOO VERY LOW
1.4. At 3-year follow-up	1	122	RR[M-H, Random, 95% CI]	0.68 (0.53,0.85)	⊕OOO VERY LOW
1.5. At 4-year follow-up	1	122	RR[M-H, Random, 95% CI]	0.57 (0.45,0.73)	⊕OOO VERY LOW
1.6. At 5-year follow-up	1	122	RR[M-H, Random, 95% CI]	0.49 (0.37,0.63)	⊕OOO VERY LOW
2. Drinking frequency					
2.1. Mean days of alcohol intoxication (non-RCT)	1	537	STD mean difference (IV, Random, 95% CI)	-0.07 (-0.25,0.11)	⊕⊕OO LOW
2.2. Days any alcohol use at 6-month follow-up	2	551	STD mean difference (IV, Random, 95% CI)	-0.10 (-0.40,0.20)	⊕⊕⊕⊕ HIGH
2.3. Days using alcohol since last interview at 6-month follow-up	1	193	STD mean difference (IV, Random, 95% CI)	-0.34 (-0.63,-0.05)	⊕⊕⊕⊕ HIGH
2.4. Days drinking any alcohol in last 30 days at 9-month follow-up	1	358	STD mean difference (IV, Random, 95% CI)	-0.13 (-0.34,0.08)	⊕⊕⊕⊕ HIGH
2.5. Days drinking any alcohol in last 30 days at 12 month follow-up	1	193	STD mean difference (IV, Random, 95% CI)	-0.21 (-0.49,0.08)	⊕⊕⊕⊕ HIGH
2.6. Days using any alcohol since last interview at 12-month follow-up	1	193	STD mean difference (IV, Random, 95% CI)	-0.30 (-0.59,-0.01)	⊕⊕⊕⊕ HIGH
2.7. Days drinking any alcohol in last 30 days at 18-month follow-up	1	193	STD mean difference (IV, Random, 95% CI)	-0.33 (-0.62,-0.05)	⊕⊕⊕⊕ HIGH
2.8. Days using alcohol since last interview at 18-month follow-up	1	193	STD mean difference (IV, Random, 95% CI)	-0.49 (-0.78,-0.20)	⊕⊕⊕⊕ HIGH

5.6.5 Clinical evidence summary

Case management versus treatment as usual

There was a significant difference in lapse (non-abstinence) at 6 month follow-up, in favour of case management, with a small effect size; however this effect was not significant at 12 month follow-up. There was a significant difference favouring case management found at 3, 4, and 5-year follow-up with the largest effect size occurring at 3 year follow-up and decreasing to a moderate effect size at 4 and 5 year follow-up, respectively. It is important to note that these results are based on one observational study (PATTERSON1997).

On measures of drinking frequency, when considering the number of days drinking any alcohol (in the last 30 days), or mean days of intoxication, there were no significant differences between case management or treatment as usual at either 6 or 12 month follow-up. Interestingly, there was a significant effect observed at 18 month follow-up in favour of case management (very small effect size) based on the results of one study (COX1998).

When considering the number of days using alcohol since the last interview (COX1998), there was a significant difference observed, favouring case management over treatment as usual at all follow-up points (small to moderate effect sizes): 6 month, 12 month follow-up and 18 month follow-up.

Based on the GRADE methodology outlined in Chapter 3, the quality of this evidence is *moderate,* therefore further research is likely to have an important impact on our confidence in the estimate of the effect (see Table).

Due to the heterogeneous nature of studies within case management, it was not possible to combine the outcome data provided across studies. As a result, there are a number of useful RCT studies which add value to the meta-analysis presented. For the purpose of this guideline, and in order to obtain a better overview of the available literature, four RCT studies (Chutuape *et al*., 2001; Gilbert, 1988; Krupski *et al*., 2009; Sannibale *et al*., 2003; Stout *et al*., 1999), which met methodological criteria but did not have usable outcomes for this review, are described below.

Gilbert (1988) conducted a randomised controlled trial comparing case management, a home visit, and treatment as usual for those with alcohol dependence. After receiving inpatient or outpatient treatment, patients were scheduled to have a case manager or a home visit, which consisted of appointments not scheduled at the hospital, but at a convenient location for the patient. Patients in the home visit condition were contacted with follow-up letters to reschedule aftercare appointments. In the traditional treatment (treatment as usual), no active attempts were made to improve attendance at aftercare appointments. On appointment keeping measures, results from an ANOVA revealed a significant group by time interaction $F=4.56(6,240)$ $p<0.01$, and post-hoc Tukey's HSD test revealed significant differences between home visit and case manager groups at 6 ($p<0.05$), 9 and 12 month follow-up ($p<0.01$). Both active treatment groups showed a decline in appointment keeping rates after the therapists stopped making active attempts to encourage the patient to attend therapy. On drinking outcomes, there were no significant differences between groups at any follow-up point.

Stout and colleagues (1999) conducted a randomised controlled trial comparing case monitoring versus treatment as usual for those with alcohol dependence. The results indicated a significant difference on percentage of days heavy drinking at 3 year follow-up, wherein the frequency of heavy drinking was twice as high in the controls as in the case monitored participants. In addition, survival analysis indicated that case monitoring was significantly better at prolonging time to lapse and relapse ($p=0.05$), as well as in reducing the severity of the relapse. There was no significant difference between the two groups for time to first heavy drinking day ($p=0.1$). It should be noted that 66% of this sample had a comorbid Axis 1 diagnosis.

Chutuape and colleagues (2001) looked at the transition from an assisted withdrawal programme to aftercare. Participants were randomly assigned to one of three conditions: incentive and escort to aftercare, incentive only, or standard treatment. Standard treatment participants only received referral instructions and were told to go to aftercare following discharge. Results from a logistic regression analysis indicated that aftercare contact rates differed significantly by referral condition ($p=0.001$). Post hoc tests indicated that participants in the escort and incentive and incentive only conditions completed intake at aftercare more ($p<0.05$) than those receiving standard treatment.

When comparing a structured aftercare programme with an unstructured aftercare programme, Sannibale and colleagues (2003) found that structured programmes had a fourfold increase in aftercare attendance (OR 4.3, 95% CI 1.7-11.2)and a reduced rate of uncontrolled substance use at follow-up (OR 0.3, 95% CI 0.1 – 0.9). Furthermore, participants in either aftercare condition relapsed later than those who attended no aftercare programme; however this significant difference did not emerge for time to lapse.

More recently, Krupski (2009) evaluated the impact of recovery support services (including case management) provided through an access to recovery programme in the US for clients undergoing substance abuse treatment. Standard treatment consisted of chemical dependency treatment. The comparison group was a multi-modal programme entitled Access to Recovery (ATR), which included a case management component. They found that, in comparison to standard care, the Access to Recovery programme was associated with increased length of stay in treatment and completion of treatment (42.5 days longer). Furthermore, multivariate survival analysis indicated the risk of ending treatment was significantly lower (hazard ratio = 0.58, $p<0.05$) among the ATR clients.

5.7 Assertive community treatment

5.7.1 Introduction

Assertive community treatment (ACT) is a method of delivering treatment and care which was originally developed for people with serious mental illness in the community (Thompson *et al.*, 1990). The intention is to prevent or reduce admission to hospital. The model of care has been defined and validated, based upon the consensus of an international panel of experts (McGrew *et al.*, 1994; McGrew & Bond, 1995). Over time the focus has shifted to provide for effective support in the community to those with severe, long-term mental illness who may previously have spent many years as hospital inpatients. Assertive community treatment now aims to support continued engagement with services, reduce the

extent (and cost) of hospital admissions and improve outcomes (particularly quality of life and social functioning).

The evidence for effectiveness in the international literature is strong for severe mental illness (Marshall and Lockwood, 2002), although this may in part be due to the comparator used (essentially poor quality standard care). For example ACT has been shown to be effective in the USA (Marshall and Lockwood, 2002), but less so in the UK (Killaspy *et al.*, 2006) where standard care is of a better quality. There is little evidence for the effectiveness of ACT in alcohol disorders and the evidence from the field of dual diagnosis (psychosis and substance misuse) is currently rather weak (NICE, 2011).

5.7.2 Clinical review protocol

Information about the databases searched and the inclusion/ exclusion criteria used for this section of the guideline can be found in Table 9.

Table 9. Databases searched and inclusion/exclusion criteria for clinical evidence.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs, Systematic Reviews
Patient population	Diagnosed with an alcohol use disorder (alcohol dependence) or alcohol misuse
Interventions	Assertive community treatment vs. other active interventions Assertive community treatment vs. treatment as usual
Outcomes	None specified

5.7.3 Studies considered[7]

For the purposes of this guideline the GDG adopted the definition of ACT used by Marshall and Lockwood (2002), which identified the following key elements:

- care is provided by a multidisciplinary team (usually involving a psychiatrist with dedicated sessions)
- care is exclusively provided for a defined group of people (those with severe and chronic problem)
- team members share responsibility for clients, so that several members may work
- with the same client, and members do not have individual caseloads (unlike case management)
- the team attempts to provide all the psychiatric and social care for each service user, rather than making referrals to other agencies
- care is provided at home or in the workplace, as far as possible
- treatment and care are offered assertively to uncooperative or reluctant service users ('assertive outreach')
- medication concordance is emphasised.

[7] Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

The review team conducted a new systematic search for RCTs and systematic reviews that assessed the benefits and downsides of assertive community treatment methods.

Four trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on 706 participants. Of these, none were unpublished and three were published in peer-reviewed journals between 1991 and 2008. In addition, two studies were excluded. The most common reason for exclusion was due to a comorbid sample population of psychosis (where this was the primary diagnosis) and alcohol dependence/misuse. Summary study characteristics of the included studies are presented in Table 5 (further information about both included and excluded studies can be found in Appendix 16b).

A meta-analysis was not performed as there was only one trial which concerned alcohol misusers as the primary group (Passetti *et al.*, 2008). The other three RCTs, Drake *et al.*, (1998), Bond & McDonald (1991) and Essock *et al.*, (2006) include populations with co-existing and primary diagnosis psychosis and substance misuse, and thus have been covered in another NICE guideline currently in development on Psychosis and Substance Misuse (NICE, 2011). It is important to note that in the Bond & McDodonald (1991) study, 70% had a primary diagnosis of schizophrenia or schizoaffective disorder and 61% reported their primary substance abuse problem was with alcohol. Conversely, in the Essock *et al.*, (2006) study, 76% had a primary diagnosis of schizophrenia or schizoaffective disorder, and 74% misused alcohol, while 81% used other substances. In the Drake *et al.*, (1998) study, 53.4% had a primary diagnosis of schizophrenia, 22.4% of schizoaffective disorder, 24.2% of bipolar, and 72.6% of the sample abused alcohol. No differences were reported in any of the 3 trials on relapse outcomes, and there were no significant differences reported on hospitalisation or relapse rates in the Essock *et al.*, (2006) or Drake *et al.*, (1998) trials, both comparing ACT with case management. In the Bond (1991) trial, there were significant differences in treatment engagement and completion of assessment, but no significant differences between groups on drinking outcomes.

5.7.4 Clinical evidence for assertive community treatment

Passetti *et al.*, (2008) conducted a parallel cohort trial comparing a flexible access clinic (based on ACT principles) with a usual care clinic. Treatment as usual (usual care clinic) consisted of 2 specialist alcohol community nurses and social workers. Medical cover was provided by a consultant, associate specialist, and a junior doctor. Care coordinators had a relatively large caseload and there was limited integration of health and social care staff, along with less community based assessments and case discussions. The trial found that participants in the flexible access clinic were significantly more likely to complete withdrawal (Pearson's Chi square test, $\chi^2 = 4.43$ $p=0.05$) enter an aftercare programme earlier (Student's t-test, $t = 2.61$, $p=0.02$). No significant differences between the two groups were found on drinking outcomes or completion of assessment.

5.7.5 Clinical evidence summary

The review of ACT failed to find any robust evidence of the effectiveness of ACT. Only one observational study provided any evidence of effectiveness.

Table 10: Characteristics of studies evaluating assertive methods

Study	Study design	Comparisons	Outcomes	Baseline severity	Treatment characteristics	Results
PASSETTI2008 (UK)	Non-randomised parallel cohort pilot study	Flexible access clinic (Assertive community treatment methods) Usual care clinic	% Completed assessment % completed aftercare % completed medically assisted withdrawal	Alcohol units per week (m, SD): Flexible access: 143(111) Usual care: 177(120)	**Flexible access clinic(n=188)**:2 walk-in weekly slots each of 3h, 2 FT CPN's, social workers, clinical psychologists and medical cover provided by staff of Community alcohol team. Offered community based assessments whenever patients had failed to attend. Modelled on ACT in the sense that it targeted patients with a history of disengagement; maintained a small case load; operated proactively and engaged assertively; it offered a flexible access including assessment and treatment in the community where required; run by a CPN care coordinator working within a multidisciplinary team that met frequently, typically after each assessment or review. **Usual care clinic (n=223)**: 2 FT specialist CPNs and 2 social workers. Full time medical staff; large caseload (25-30), multidisciplinary case discussion took place once weekly or less, community based assessments were not offered and limited integration of health and social care staff work	No significant differences between the two groups on % completing assessment. Significant differences found between two groups on % completed withdrawal programmes, $p<0.05$ (fin favour of flexible access clinic,) and % entered aftercare, $p<0.02$)

5.8 Stepped care

5.8.1 Introduction

The stepped care approach to care is based on two key principles (Davison, 2000; Sobell and Sobell, 2000):

- The provision of the least restrictive and least costly intervention that will be effective for a person's presenting problems.
- The use of a self-correcting mechanism which is designed to ensure that if an individual does not benefit from an initial intervention a system of monitoring is in place to identify a more appropriate and intensive intervention is provided.

Stepped care models, which have their origins in the treatment of tobacco addiction (Sobell and Sobell, 2000), provide for escalating levels of response to the complexity or severity of the disorder and are an explicit attempt to formalise the delivery and monitoring of patient flows through the system. In establishing a stepped-care approach, consideration should be given not only to the degree of restrictiveness associated with a treatment and its costs and effectiveness, but also the likelihood of its uptake by a patient and the likely impact that an unsuccessful intervention will have on the probability of other interventions being taken up. Despite the origins in the field of addiction, stepped care systems have not been the subject of much formal evaluation in the area. A useful review by Bower and Gilbody (2005) of the evidence for the use of stepped care in the provision of psychological therapies generally was unable to identify a significant body of evidence. However, they set out three assumptions which they argue a stepped-care framework should be built on and which should be considered in any evaluation of stepped care. These assumptions concern the equivalence of clinical outcomes (between minimal and more intensive interventions, at least for some patients), the efficient use of resources (including healthcare resources outside the immediate provision of stepped care) and the acceptability of low-intensity interventions (to both patients and professionals). They reviewed the existing evidence for stepped care against these three assumptions and found some evidence to suggest that stepped care may be a clinically and cost-effective system for the delivery of psychological therapies, but no evidence that strongly supported the overall effectiveness of the model.

In the field of alcohol misuse there are well-developed, brief intervention which are suitable for use in a stepped care system (see NICE, 2010a for a comprehensive review) such as brief motivational interventions, but other low-intensity interventions which are less dependent on the availability of professional staff and focus on patient-initiated approaches to treatment are also available and include self-help materials such as books and computer programmes (Bennet-Levey *et al.*, 2010). In addition, many alcohol treatment services already operate forms of stepped care and they are implicit in current national policy guidance (MoCAM; DH, 2006) but as yet there has been little formal evaluation or systematic review of the area.

Definition

For the purposes of this review, stepped care is defined as a system for the organisation and delivery of care to people with harmful or dependent drinking which:

a) Provides to the majority, if not all harmful or dependent drinkers, the least restrictive and least costly brief interventions that will be effective for a person's presenting problems.
b) Has a system of built-in monitoring which ensures that those who have not benefited from the initial intervention will be identified
c) Has the referral systems and capacity to ensure that more intensive interventions are provided to those which have not benefited for a low intensity intervention.

5.8.2 Clinical review protocol

Information about the databases searched and the inclusion/exclusion criteria used for this section of the guideline can be found in Table 6 (further information about the search for health economic evidence can be found in Section 5.8.5).

Table 11: Databases searched and inclusion/exclusion criteria for clinical evidence.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs, Systematic Reviews
Patient population	Those with alcohol dependence or alcohol misuse
Interventions	Stepped care approach vs. Treatment as Usual
Outcomes	Any drinking outcome Engagement or attendance in aftercare sessions or programmes

5.8.3 Studies considered[8]

The review team conducted a new systematic search for RCTs and observational studies that assessed the benefits and downsides of stepped care approaches.

Three trials relating to clinical evidence that potentially met the eligibility criteria set by the GDG were found, providing data on 496 participants. Of these, three (Bischof, 2008, Breslin *et al.*,1999, Drummond *et al.*, 2009) were published in peer-reviewed journals between 1999 and 2009. The trials are listed below in Table 7 and the outcomes of the studies are described in the text below. The GDG considered these studies very carefully and concluded that, despite the claims of individual studies (for example, labelling the intervention as stepped care), and none of studies delivered a form of stepped care that was fully consistent with the definition of a stepped care approach adopted for this guideline.

[8] Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

Table 12. Characteristics of Studies Evaluating Stepped Care Approaches

Study	Study Design	Comparisons	Outcomes	Baseline Severity	Treatment Characteristics	Results
DRUMMOND2009 (UK)	RCT	Stepped care intervention Minimal intervention (Control)	Total alcohol consumed in 180 days Drinks per drinking day Percent days abstinent	Total alcohol consumed in 180 days (mean, SD) Intervention: 1699.6(194.8) Control: 1423(113.3) DDD Intervention: 15.2(1.1) Control: 12.9(0.8) PDA Intervention: 37.9(3.8) Control: 36.6(3.4)	**Intervention**: (n=39): Sequential series of interventions according to need/response. Step 1: 40-min session of behaviour change counselling from a nurse with follow-up 28 days after initial session. Patients consumed >21 units of alcohol in any 1wk or >10 units/day referred to step 2. Step2: 4 x 50-min sessions of MET (trained alc. Counsellor), follow up 28 days. If consumed same as above, step 3. Step 3: Referral to local community alcohol team for specialist intervention. No limit on duration /intensity of treatment, where necessary, assisted withdrawal, inpatient treatment, outpatient counselling, RP and drug therapy given. **Control:** (n=52): 5-minute directive advice session from practice nurse addressing alcohol consumption reduction. Received Self-help booklet. `	Greater reduction in stepped care group than control in total alcohol consumed (-408.6g vs. -238.8g) and DDD (-2.4 v -1.0) with an adjusted mean difference of 145.6 (95% CI -101.7 to 392.9) and 1.1 (-0.9 to 3.1) but not significant.
BRESLIN1999 (CANADA)	RCT	Stepped Care approach (Treatment non-responders assigned to 3 groups based on whether they were heavily drinking or not)	Percent days abstinent Drinks per drinking day	Alcohol Dependence Scale score: Range: 11.3 – 12.8	**Initial treatment**: 4 sessions of motivationally based outpatient treatment. Treatment non-responders who consumed more than 12 drinks per week between assessment and 3rd session received were considered to be "drinking heavily during treatment" an additional "step", which consisted of additional readings, written exercises and a personalised progress report. N=67 responded to initial treatment N=33 received supplemental intervention N=36 did not respond to initial treatment	No significant differences between groups for PDA or DDD due to having a supplemental intervention. MANOVA indicated a significant effect of time for PDA, F (2, 116= 35.89, p<0.0001, for all groups) DDD F(,2,115) = 26.91, p<0.0001.

Note: PDA: Percent days abstinent; DDD: Drinks per drinking day

Study	Study Design	Comparisons	Outcomes	Baseline Severity	Treatment Characteristics	Results
BISCHOF2008 (GERMANY)	RCT	Stepped care Full care Untreated Control Group	Grams of alcohol per day at follow-up	Grams of alcohol per day CG: Overall: 41.0 (50.3) SC: 46.9(49.3) FC: 49.0(41.3)	**Full care**: (n=131) Received a computerised feedback. Received brief counselling sessions based on motivational interviewing and behavioural change counselling , each session 30 minutes **Stepped care**: (n=138) Computerised intervention and maximum of 3 brief counselling sessions at 1, 3, 6 months after baseline. 30-40 minutes each. If a participant within the SC group reported a reduction of alcohol consumption below the study criteria for at risk drinking and binge drinking within the last 3 weeks and also indicated a high self-efficacy to keep the acquired behavioural change up, the intervention was discontinued and no further contact made until 12 month follow-up. **Control:** (n=139) Received a booklet on health behaviour.	No significant differences except when split by severity, where at-risk drinkers were significantly different from the control group on difference in grams alcohol per day baseline to follow-up (Mann-Whitney U test, p=0.002) and binge criteria at FU, Mann-Whitney U test, p=0.039) OLS-regression: no significant difference, overall, (r^2 change =0.006, p=0.124) A sig. difference for at risk/alcohol misusers (r^2 change = 0.039, p=0.036) but not for alcohol dependence (r^2 change = 0.002, p=0.511) or heavy episodic driving (r^2 change = 0.000, p=0.923)

5.8.4 Clinical evidence for stepped care

Breslin *et al*., (1997) evaluated the contribution of pre and within treatment predictors with 212 problem drinkers who initially completed a brief cognitive behavioural motivational outpatient intervention. The analyses revealed that in the absence of the ability to systematically monitor within treatment drinking outcomes and goals, therapist prognosis ratings can be used in making stepped care treatment decisions. These prognosis ratings improve predictions of outcomes even after pre-treatment characteristics are controlled. In a later study, Breslin *et al*., (1998) evaluated a stepped-care model (but which the GDG considered might be more accurately described as an evaluation of sequenced as opposed to stepped care) for harmful drinkers, with the initial treatment consisting of four sessions of motivationally-based outpatient treatment. The design split participants into treatment responders and non-responders, with treatment non-responders defined as those having consumed >12 drinks per week between assessment and the third session of the intervention. There was also a third group of non-responders who did not respond to initial treatment, but received a supplemental intervention consisting of post-treatment progress reports. A repeated measures ANOVA indicated a significant effect of time for percent days abstinent (PDA), F (2, 116= 35.89, p<0.0001, for all groups) and for drinks per drinking day (DDD), F (2,115) = 26.91, p<0.0001. F Results from follow-up contracts revealed that those who received a supplemental intervention showed no additional improvements on drinking outcome measures in comparison to those who did not receive a supplemental intervention (no significant differences on PDA or DDD). Furthermore, treatment responders and non-responders sought additional help at the same rate. It must be noted that this intervention and approach was aimed at problem drinkers and not at severely dependent drinkers. Furthermore, it is possible that the lack of effect in this study was due to the intensity of the "stepped" intervention, as it only consisted of a progress report. It is possible that we could increase our confidence in the effect if the supplemental intervention provided to treatment non-responders from the initial intervention was more intensive and alcohol-focused.

Bischof (2008) compared two types of stepped care interventions (but which the GDG consider to be a comparison of two different models of brief interventions) with a control group. The stepped care group received a computerised feedback programme after assessment and a maximum of 3 brief counselling sessions delivered by telephone, lasting 30 to 40 minutes each. The counselling was delivered based on the success of the previous intervention, the computerised feedback programme. If a participant reported a reduction of alcohol consumption, the intervention was discontinued. Those in the full care group received a fixed number of 4 telephone-based brief counselling sessions at 30 minutes each, in addition to the computerised feedback system. The control group received a booklet on health behaviour. An OLS regression analysis indicated that there was no significant difference overall, in terms of efficacy of the intervention (r^2 change =0.006, p=0.124). A significant difference was found for at risk/alcohol misuse at 12 month follow-up (r^2 change = 0.039, p=0.036) but not for alcohol dependence (r2 change = 0.002, p=0.511) or heavy episodic driving (r^2 change = 0.000, p=0.923). Thus, stepped care and full care groups did not differ on drinking outcomes, but when compared to control, the intervention showed small to medium effect size for at-risk drinkers

only. It should be noted that this intervention does not fit with the definition of stepped care used for this guideline, as the approach employed in this study represents more intensive levels of the same interventions, rather than 'stepped' up care if the participant does not respond to the initial intervention.

More recently, Drummond and colleagues (2009) conducted an RCT pilot study to evaluate a stepped care intervention in primary care primarily for hazardous and harmful drinkers (and in the view of the GDG not a stepped care model with much relevance to the population which is the focus of this guideline), compared to a minimal intervention. Participants received either a 3 stage stepped care intervention, or a 5 minute of brief advice delivered by a practice nurse. Participants in the stepped care intervention received a single session of behaviour change counselling (delivered by a practice nurse), four 50-minute sessions of motivational enhancement therapy (MET) provided by an alcohol counsellor, and lastly, referral to a community alcohol treatment agency. At 6 month follow-up, there was a reduction on drinking outcome measures in both groups, and a slight trend favouring the stepped care intervention, for total alcohol consumed (adjusted mean difference =145.6, 95% CI= -101.7- 392.9, effect size difference = 0.23) and drinks per drinking day (Adjustment mean difference=1.1, 95% CI = -0.9 -3.1, effect size difference =0.27). These differences were not significant.

5.8.5 Health economic evidence

The study by Drummond and colleagues (2009) included a cost-effectiveness analysis of a stepped care alcohol intervention compared to minimal intervention in the primary care setting. The study population consisted of UK males with a diagnosis of an alcohol use disorder and follow-up was six months post-randomisation. The primary outcome measure used in the economic analysis was the QALY, estimated from EQ-5D utility scores obtained from the study participants. A societal perspective was adopted for the analysis which included costs relating to staff training, specific psychological interventions, other health and social care and criminal justice services. In the intervention group, mean total costs were £5,692 at baseline and £2,534 at follow-up, compared with £6,851 and £12,637 in the control group. At 6 months, the intervention group had gained a mean 0.3849 QALYs compared with 0.3876 in the control group. Therefore, the control group was both more costly and more effective in comparison with the intervention group, although the difference in effectiveness was not statistically significant. The authors calculated that, at a UK cost-effectiveness threshold range of between £20,000 to £30,000 per QALY, stepped care has a 98% probability of being the most cost-effective option. The results from this study are directly applicable to UK clinical practice and the primary outcome measure ensures comparability across health care interventions. However, potential limitations include the small sample size which limits the ability to detect statistically significant differences in costs and outcomes, and the short time horizon of the study. In addition, no sensitivity analyses were carried out to test the robustness of the cost-effectiveness results.

5.8.6 Health economics summary

Only one study was identified that considered the cost-effectiveness of a stepped care approach to the management of alcohol use disorders (Drummond *et al*., 2009). The initial results of this short-term pilot study suggest that stepped care may offer significant cost savings without any significant impact on health outcomes over six

months. Further, longer term trial based evidence is required to confirm the cost-effectiveness of stepped care beyond six months.

5.9 From evidence to recommendations

5.9.1 Case management

The evidence suggests that case management is equally as effective as another active intervention (for example, home visits) in maintaining abstinence. Evidence from both randomised and observational trials indicates that when case management is compared to standard treatment, case management is significantly better than treatment as usual in reducing lapse, alcohol use, and in promoting engagement and completion of treatment and aftercare. In terms of aftercare, the components of aftercare and outcome measures vary widely across studies. There are many ways of motivating a patient to engage in aftercare programmes, and of structuring an aftercare programme in an attempt to retain the patient. These include the use of incentives, having access to an escort for aftercare sessions, being prompted and contacted by an aftercare therapist, and having structured aftercare programmes. The GDG considered case management to be an effective but relatively intensive intervention of people with alcohol misuse problems. Given the positive response to a range of psychosocial interventions by people who are harmful alcohol users or who are suffering from mild dependence to interventions such as cognitive behaviour therapy, or social network and behaviour therapy in the presence of standard case coordination, the GDG felt that case management should be targeted at those with moderate and severe dependence and in particular those who have a history of difficulty in engaging with services. The GDG were also aware that case coordination is part of routine care (see the introduction to this chapter) in all alcohol services but were concerned that the focus of case management is only on the more severely alcohol dependent and that as a consequence that the coordination of care for harmful alcohol misuse and those with mild alcohol dependence were at risk of the coordination of their care being neglected. This was a particular concern, given the considerable number of agencies involved in the delivery of alcohol misuse services. In order to address this issue the GDG made a recommendation for the delivery of case coordination.

5.9.2 Assertive community treatment

Although assertive community interventions have been reviewed in another NICE guideline under development for psychosis and substance misuse (NICE, 2011), the narrative review of these studies in this guideline identified a very limited evidence base. In this review one trial assessing assertive community treatment versus standard care suggested that assertive methods may be beneficial in improving rates of completion and attendance in medically-assisted withdrawal and aftercare programmes. On the basis of this single trial, there is insufficient evidence to reach to support any clinical recommendation but the GDG did develop a research recommendation as it considered that the ACT might have value in ensuring more effective care and treatment for severely alcohol dependent people who have significant problems in engaging with services.

5.9.3 Stepped care

None of the studies reviewed directly addressed stepped care either as defined in the guideline or for the populations covered by this guideline. The GDG has therefore no recommendations to make which might suggest changes to the current system for stepped care that structure the provision of alcohol misuse services.

5.10 Recommendations

5.10.1.1 Care coordination should be part of the routine care of all service users in specialist alcohol services and should:

- be provided throughout the whole period of care, including aftercare,
- be delivered by staff within specialist alcohol services
- include the coordination of assessment, interventions and monitoring of progress, and coordination with other agencies.

5.10.1.2 Offer case management to increase engagement in treatment for people who are moderately to severely alcohol dependent and who are considered at risk of dropping out of treatment or who have a previous history of poor engagement. Case management should be provided throughout the whole period of care, including aftercare.

5.10.1.3 Case management should be delivered in the context of Tier 3 interventions[9] by staff who take responsibility for the overall coordination of care and should include:

- a comprehensive assessment of needs
- development of an individualised care plan in collaboration with the service user and relevant others (including families and carers and other staff involved in the service user's care)
- coordination of the care plan to deliver a seamless and individual integrated care pathway and maximisation of engagement, including the use of motivational interviewing approaches
- monitoring of the impact of interventions and revision of the care plan when necessary.

5.11 Research recommendation

5.11.1.1 For which service users who are moderately and severely dependent on

[9] See appendix C.

alcohol is an assertive community treatment model a clinically and cost-effective intervention compared with standard care?

This question should be answered using a randomised controlled design in which participants are stratified for severity and complexity of presenting problems. It should report short- and medium-term outcomes (including cost-effectiveness outcomes) of at least 18 months' duration. Particular attention should be paid to the reproducibility of the treatment model and training and supervision of those providing the intervention in order to ensure that the results are robust and generalisable. The outcomes chosen should reflect both observer and service user-rated assessments of improvement (including personal and social functioning) and the acceptability of the intervention. The study needs to be large enough to determine the presence or absence of clinically important effects, and mediators and moderators of response should be investigated.

Why this is important?

Many people, in particular those with severe problems and complex comorbidities, do not benefit from treatment and/or lose contact with services. This leads to poor outcomes and is wasteful of resources. Assertive community treatment models have been shown to be effective in retaining people in treatment in those with serious mental illness and who misuse alcohol and drugs but the evidence for an impact on outcomes in not proven. A number of small pilot studies suggest that an assertive community approach can bring benefit in both service retention and clinical outcomes in alcohol misuse. Given the high morbidity and mortality associated with chronic severe alcohol dependence the results of this study will have important implications for the structure and provision of alcohol services in the NHS.

Section 3 - The assessment of harmful and dependent alcohol misuse

5.12 Introduction

The purpose of this chapter is to identify best practice in the diagnosis and assessment of alcohol misuse across a range of clinical settings. Previous reviews of assessment procedures (for example, Raistrick *et al*, 2006; Allen and Wilson, 2003) have outlined the role of clinical interview procedures, identification questionnaires and investigations in developing an assessment of needs. The purpose of this chapter is to identify best practice in the assessment of alcohol misuse for NHS provided and funded services, including primary care and non-statutory alcohol services. In order to obtain a comprehensive overview of the range and variety of assessment procedures this chapter should be read in conjunction with the reviews and recommendations on identification and assessment contained in two other NICE guidelines on alcohol misuse (NICE, 2010a; NICE 2010b).

A key aim of the assessment process should be to elicit information regarding the relevant characteristics of alcohol misuse as outlined in the current diagnostic systems for alcohol use disorders; that is the World Health Organisation's International Classification of Mental Disorders, 10th Revision (ICD-10; WHO, 1992) and the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-IV, APA 1994). Although diagnosis is an important aspect of most assessments the focus of assessment should not only be on diagnosis and alcohol consumption, but should also consider physical, psychological and social functioning. The range and comprehensiveness of any assessment will vary depending on the setting in which it is undertaken and the particular purpose of the assessment but in all cases the central aim is to identify a client's need for treatment and care. The comprehensiveness of the assessment should be linked to the intended outcomes (for example, onward referral of an individual or offering treatment interventions). The range and depth of the components of assessment should reflect the complexity of tasks to be addressed and the expertise required to carry out the assessment. Crucial to the effective delivery of any assessment process is the competence of the staff who are delivering it, including the ability to conduct an assessment, interpret the findings of the assessment and use these finding to support the development of appropriate care plans and where necessary risk management plans.

Current practice in the assessment of alcohol misuse is very varied across England and Wales, including the range of assessments in specialist alcohol services (MOCAM, DH 2006). To some extent this reflects the different aims and objectives of the services (including specialist alcohol services) in which assessments are undertaken but it also reflects the lack of clear guidance and subsequent agreement on what constitutes the most appropriate assessment methods for particular settings (MOCAM, DH 2006). Given the high prevalence of alcohol misuse and their comorbidity with a wide range of other physical and mental disorders, it is apparent that effective diagnosis and assessment can have major implications for the nature of any treatment provided and the likely outcome of that treatment. In an attempt to address some of these concerns the National Treatment Agency (NTA) developed

the Models of Care for Alcohol Misusers (MoCAM; DH, 2006) which outlined a four-tiered conceptual framework for treatment and describes three levels of assessment (a screening assessment, a triage assessment, and a comprehensive assessment) that should be considered in different clinical settings. However, the extent to which this framework has led to improvements in the nature and quality of assessments provided remains unclear (but it has been more influential in determining the structure of services. The importance of the MoCAM document for this chapter (and for the guideline in general) is that it provides a conceptual framework in which to place the recommendations on assessment and which also link with the recommendation on assessment in the other NICE guidelines on alcohol (NICE, 2010a; NICE 2010b). With this in mind the GDG decided to develop a set of recommendations for assessment which supported the development of clinical care pathways to promote access to effective care, where possible integrating with the existing service structure. Where this is not possible the GDG has developed recommendations which suggest changes in existing service structures.

5.13 Clinical questions

The clinical questions which the GDG addressed, and from which the literature searches were developed were:

a) What are the most effective a) diagnostic and b) assessment tools for alcohol dependence and harmful alcohol use?

b) What are the most effective ways of monitoring clinical progress in alcohol dependence and harmful alcohol use?

c) To answer these questions, what are the advantages, disadvantages, and clinical utility of:
   - The structure of the overall clinical assessment
   - Biological measures
   - Psychological/behavioural measures
   - Neuropsychiatric measures (including cognitive impairment)
   - Physical assessment?

5.14 Aim of review of diagnostic and assessment tools for alcohol dependence and harmful alcohol use

5.14.1 Introduction

This review aims to identify the most appropriate tools for assessing the presence of alcohol dependence or harmful drinking, the severity of dependence, alcohol consumption/frequency of use, motivation and readiness to change, alcohol withdrawal and alcohol-related problems in adults. (The issue of assessment in children aged 10 to 18 years is dealt with in Chapter 6.) The GDG were also tasked with identifying all the potential components of a clinical assessment (and their respective places in the care pathway) which would facilitate the most effective delivery of any assessment. This section sets out the criteria for a quantitative analysis of the assessment tools included in the review and the subsequent synthesis of the characteristics and psychometric properties of the tools.

5.14.2 Clinical review protocol

Information about the databases searched and the inclusion/exclusion criteria used for this section of the guideline can be found in Table 13.

Table 13. Clinical review protocol for the evaluation of tools for assessing alcohol dependence and harmful alcohol use

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs, Systematic Reviews
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Assessment domains	Dependence (and severity of dependence), consumption/frequency, alcohol withdrawal, motivation and readiness to change, physical, psychological and social problems, clinical interview, physical examination, blood, breath and urine testing
Critical outcomes	Critical Outcomes for quantitative review: Sensitivity, specificity, area under the curve, positive predictive value, negative predictive. For quantitative meta-analyses calculating the diagnostic accuracy of an assessment tool, raw data (true positive, true negative, false positive, false negative) is needed. See methods chapter 3 for a definition of these terms.

5.15 Quantitative review of assessment tools

5.15.1 Aim of a quantitative review of assessment tools

The initial aim of this review was to assess the pooled diagnostic accuracy of the assessment tools using meta-analytic Receiver Operating Characteristic Curve (ROC) analyses. ROC analyses would therefore provide the pooled sensitivity and specificity of each assessment tool and give an indication of positive predictive value and negative predictive value. For a definition and explanation of these terms see Chapter 3.

5.15.2 Evaluating assessment tools for use in a review to assess diagnostic accuracy

The review team conducted a systematic review of studies that assessed the psychometric properties of all alcohol related assessments tools. From these, references were excluded by reading the title and/or abstract. At this stage of the sifting process, studies were excluded if they did not address the diagnostic accuracy of an assessment tools and hence were not relevant for this section of the review. Furthermore, the focus of this review was on assessment and not screening or case identification (latter issues are covered in NICE guideline on preventing hazardous and harmful drinking, 2010). Therefore, tools developed solely for those purposes were excluded from the review. The remaining references were assessed for eligibility for use in meta-analyses on the basis of the full text using certain inclusion

criteria and papers excluded if they did not meet said criteria. The inclusion criteria were as follows:

- The study meets basic guideline inclusion criteria (see chapter 3).
- The population being assessed in the study reflects the scope of this guideline (see Table 8).
- Extractable data needed to perform pooled sensitivity and specificity analyses (see methods chapter 3).
- The assessment tool is tested against a validated gold standard diagnostic instrument (for example, DSM-IV, ICD-10, Comprehensive International Diagnostic Interview (CIDI) (APA, 1994; WHO, 1992).

5.15.3 Outcome of study search for quantitative review

Following the sifting process as outlined above, 33 studies assessing the diagnostic accuracy of a wide range of assessment tools were identified for possible inclusion in meta-analyses. Twenty seven studies were excluded and could not be used for a quantitative review. The main reason for this was that the population being assessed were outside the scope of this guideline (for example, pregnant women, hazardous drinkers, less than 80% of the sample were alcohol dependent or abusers). Studies were further excluded because they did not report sensitivity and specificity data in an extractable format.

After all exclusion criteria were applied, there were only six studies remaining which could have been used for a quantitative review. This number of studies was insufficient to perform an unbiased and comprehensive diagnostic accuracy meta-analyses of for all the assessment tools identified in the review for alcohol misuse. Although there were a wide range of tools initially identified for the meta-analyses, most studies did not provide appropriate psychometric information and the majority of studies reported the results of their own sensitivity and specificity analyses. As outlined above, the actual number of participants identified as TP, TN, FP, FN (see chapter 3 for definition) is needed to run pooled sensitivity and specificity analyses.

In view of the limitations of the data it was therefore decided by the GDG that a narrative synthesis of assessment tools should be undertaken. Therefore, all papers were reconsidered for use in a narrative review.

5.16 Narrative synthesis of assessment tools

5.16.1 Aim of narrative synthesis

The main aim of the narrative synthesis was to identify tools that could inform clinical decision making and treatment planning in the following areas: the assessment of alcohol dependence; the severity of alcohol dependence and the associated harms; and motivation for change. This guideline did not aim to review assessment tools to aid in the measurement of alcohol withdrawal as these tools have already been reviewed in the accompanying NICE guideline on management of alcohol-related physical complications (NICE, 2010b), which recommends the use of the Clinical Institute Withdrawal Assessment Scale for Alcohol (CIWA-Ar) (Sullivan *et al*., 1989). To facilitate understanding and use of the CIWA-Ar, its characteristics can be seen in Table 9 and Table 10.

5.16.2 Evaluating assessment tools for use in a narrative synthesis

The inclusion and exclusion criteria of the initial sifting process were reapplied to the available literature and involved identifying assessment tools which were applicable to the population of interest in this guideline. The literature was evaluated for a number of important study characteristics and assessment tools/literature were excluded on this basis. Firstly, the patient population was required to meet inclusion criteria for alcohol misuse, that is, harmful or dependent drinkers. Furthermore, the psychometric data for the study was required to adequately distinguish between alcohol misuse and substance misuse in an adult dual-diagnosed sample. The context in which the tool is used was also evaluated, that is, to ascertain if the tool is used for generic screening only (see NICE guideline on preventing hazardous and harmful drinking, 2010) or can be used for assessment of dependence and outcome monitoring in a treatment-seeking population.

The second stage of the review was to identify tools for a narrative which could be recommended for use in assessing alcohol misuse in a clinical setting. In the absence of a formal quantitative review, the decision to include assessment tools in a narrative synthesis was made using the three criteria outlined below. These criteria were developed and agreed by the GDG and informed by the NIAAA guide for assessing alcohol problems (Allen & Wilson, 2003).

Clinical Utility: This criterion required the primary use of the assessment tool to be feasible and implementable in a routine clinical care. The tool should contribute to the identification of treatment needs and therefore be useful for treatment planning.

Psychometric Data: Reported findings for sensitivity, specificity, area under the curve, positive predictive value, negative predictive value, reliability and validity of the assessment tools were considered. Although sensitivity and specificity are important outcomes in deciding on the usefulness of an assessment tool, particularly for diagnostic purposes, for other clinical purposes reliability and validity are also important. See Chapter 3 for a description of different types of reliability and validity. The tool should be applicable to a UK population, for example by being validated in a UK population, or a population that is similar to the UK population.

Tool characteristics and administrative properties: The assessment tool should have well validated cut-offs in the patient population of interest. Furthermore, and dependent on the practitioner skill-set and the setting, tools were evaluated for the time needed to administer and score as well as the nature of the training (if any) required for administration or scoring. Lastly, the cost of the tool and copyright issues were also considered.

5.16.3 Outcome of the narrative synthesis

The studies initially identified were as a result of the original quantitative review search and sift. A total of seventy three tools were identified and thirty four were excluded from the review, leaving thirty nine assessment questionnaires and clinical interview tools which were considered for a narrative review.

The clinical interview tools identified did not form a part of the narrative review of assessment questionnaires. Most (n=5) were excluded as being not feasible for

routine use in a UK NHS setting (see criteria above) but those for people are considered in the Chapter 6.

The outcome of the initial sift and the exclusion criteria applied was discussed with the GDG and the preliminary list of thirty nine assessment tools were put forward for possible inclusion in the narrative synthesis. Using the additional criteria (i.e. clinical utility, psychometric data and characteristics of the tool), this discussion resulted in a sub-set of five questionnaires (excluding the CIWA-Ar) included in the subsequent narrative synthesis. Table 14 displays information pertaining to the questionnaires which met criteria for a narrative review. These tables provide information of the domain the tool assesses (for example, dependence, problems etc) and indicates if the tool is appropriate for the assessment of young people or adults. Additionally, Table 15 displays the characteristics of the assessment questionnaires included in the narrative review. This table gives more extensive information such as the scale and cut-offs, number of items, time to administer and score, if training is required for use, copyright/cost of the tool and the source reference. Table 11 identifies the questionnaires and clinical interview tools identified in the original sift but excluded for the reasons outlined above.

In developing this review the GDG were mindful of the need for all assessments and interventions to be carried out by competent individuals (for example, Krisnamurthy *et al.,* 2004; MOCAM; DH, 2006) and this chapter should be read with this clear expectation in mind. It should also be noted that the accuracy of the assessment of alcohol consumption from self-reported alcohol consumption can be enhanced (Sobell & Sobell, 2003) by interviewing individuals who are not intoxicated, giving written assurances of confidentiality, encouraging openness and honesty; asking clearly worded questions and providing memory aids to recall drinking (i.e. drinking diaries).

5.17 Assessment of alcohol dependence - review of included assessment tools

From the initial review, and using the criteria outlined in section 1.14.1, the GDG identified three measures for inclusion in the narrative review of tools to measure alcohol dependence. These were the Alcohol Use Disorders Inventory Test (AUDIT) (Babor *et al*., 2001); the Severity of Alcohol Dependence Questionnaire (SADQ) (Stockwell *et al*., 1979); and the Leeds Dependency Questionnaire (LDQ) (Raistrick *et al*., 1994). Information on the characteristics of these three questionnaires is summarised in Table 9 and Table 10

5.17.1 Alcohol Use Disorders Inventory Test (AUDIT)

The AUDIT questionnaire was developed by the World Health Organisation and designed to identify people who have an alcohol use disorder. Although the AUDIT was not primarily developed as a measure of alcohol dependence, and indeed contains items from a range of domains (including alcohol consumption and alcohol related problems), it may have utility in assessment of alcohol dependence, particularly by staff who are not working in specialist alcohol treatment services (for example, GPs and acute hospital and mental health care staff). Unlike many of the other published assessment questionnaires, previous literature assessing the psychometric properties of the AUDIT is extensive. The AUDIT has 10 items constructed across three domains: i) consumption (Items 1-3), ii) dependence (Items

4-6) and problems (7-10). The development of the AUDIT revealed that score of 16 or more represented high levels of alcohol problems. In a UK primary care sample the AUDIT at a cut off of ≥8, using CIDI as the gold standard was found to identify alcohol dependent patients with a sensitivity of 84% and specificity of 83% (Coulton *et al*, 2006). The AUDIT has a maximum score of 40 with the following categories being defined: 1-7, low-risk drinking; 8-15, hazardous drinking; 16-19, harmful drinking and 20+ possible alcohol dependence (Room & Rehm, 2005). However, for cut-offs higher than 8 (which could be used to identify harmful or dependent drinkers as opposed to hazardous drinkers), as would be expected the specificity remains much the same, the sensitivity of AUDIT appears to reduce drastically. For example at a cut-off score of 15, sensitivity for DSM-III diagnosed abuse or dependent patients was 49% (Fleming, 1991). Even at much lower cut-offs of 12 points, Barry (1993) reported a sensitivity of 21% (lifetime diagnosis) and 36% (current diagnosis). At a cut-off of 11 points, Schmidt (1995) reported a sensitivity of 11% for abuse or dependence diagnosis.

The AUDIT has been found in a number of studies and various settings and populations to have high internal consistency (Barry, 1993; Fleming, 1991; Hays, 1995; Schmidt, 1995, Thomas, 2008). However, data is not readily available on test-retest reliability bar a study in a young adult population (mean age 20.3 years) in which the authors report high test-retest reliability (Thomas 2008).

The correlation between AUDIT score and severity of dependence has been investigated in a severely dependent sample of participants (n=1134, 84.9%) scoring in the higher range of AUDIT scores (20-40 points) (Donovan, 2006). Correlation analyses results revealed that an AUDIT score of 8-15 was mostly correlated with mild (53.3%) and moderate (41.7%) severity, an AUDIT score of 16-19 was mostly correlated with moderate (55.7%) and mild (37.1%) severity, and a score of 20-40 points was mostly correlated with moderate (55.7%) and severe (29.5%) dependence. The authors conclude that AUDIT may therefore be applicable in a clinical setting for assessing severity of alcohol dependence in a treatment seeking population.

The AUDIT score categories described relate to adults. Professional judgment as to whether to revise scores downwards should be considered for; women (including those who are or planning to become pregnant), young people (under 18 years), people age 65 or over, and those with significant mental health problems (O'Hare *et al.*, 2006).

The AUDIT is predominantly used for screening purposes. However it has some clinical utility as it can be used as the basis for brief intervention or a referral to specialist services. The AUDIT is routinely used for screening in the UK and is freely available to download. Furthermore, although it requires minimal training for administration and scoring by trained personnel, it is quick and easy to use. The AUDIT manual (Babor, 2001) states that clinical judgement should be exercised when using the proposed cut-offs if other evidence presented is contrary to the AUDIT score, especially for those who have a history of alcohol dependence.

5.17.2 Severity of alcohol dependence questionnaire (SADQ)

The Severity of Alcohol Dependence Questionnaire was developed by Stockwell *et al.* (1979). It is a 20-item questionnaire with a maximum score of 60. Five elements of the alcohol dependence syndrome (Edwards & Gross, 1976) examined are:

- Physical Withdrawal (Items 1-4)
- Affective Withdrawal (Items 5-8)
- Withdrawal Relief Drinking Items (9-12)
- Alcohol Consumption Items (13-16)
- Rapidity of Reinstatement Items (17-20)

Stockwell (1983) reported that the SADQ (Stockwell *et al.*, 1979; 1983) has high test-retest reliability (correlation coefficient ranged from 0.55 to 0.82 across individual questions); good content, criterion and construct validity, and is correlated with physician and self-reported ratings of withdrawal severity and the quantity of medication to be prescribed during alcohol withdrawal. However, the SADQ questions assessing consumption and frequency of drinking did not correlate with liver function and blood tests.

SADQ scores greater than 30 indicates severe alcohol dependence (Stockwell *et al.*, 1983); with higher scores predicting increased severity of alcohol withdrawal symptoms (Saunders *et al.*, 1983; Shaw *et al.*, 1998; Stockwell *et al.*, 1983; Stockwell *et al.*, 1998; Wodak *et al.*, 1983). Severe dependence, because of the risk of severe alcohol withdrawal symptoms is often used as a clinical decision aid in deciding on the need for inpatient assisted alcohol withdrawal programmes and an inclusion criterion for inpatient care.

Severe alcohol dependence (for example, SADQ scores that are more than 30) particularly in those with comorbid problems or who lack social support (see below), may require inpatient assisted withdrawal programme (Raistrick *et al.*, 2006). The professional will need to consider if the severity of alcohol dependence and associated alcohol withdrawal symptoms identified before considering a prescribing strategy. Current clinical practice, in the experience of the GDG, suggests that those identified as scoring over 15 on the SADQ usually require medication to assist alcohol withdrawal.

The SADQ identifies not just dependence but indicates the severity of dependence and is hence applicable in a clinical setting. It is routinely used in the UK and is freely available to download or from the author. The SADQ takes very little time to administer and does not require training for administration or scoring.

5.17.3 Leeds Dependence Questionnaire (LDQ)

The Leeds Dependence Questionnaire (LDQ) (Raistrick *et al.*, 1994) is a 10-item questionnaire that is based on a psychological understanding of dependence and has applicability to the measurement of dependence for any substance. A score greater than 21 out of a possible 30 indicates severe dependence. The LDQ has been reported to have acceptable concurrent validity when compared to other instruments such as the SADQ ($r = 0.69$, $p<0.0001$); is independent of other possible covariates such as gender and age, have high internal consistency (one factor accounted for 64.2% of the variance), and high test-retest reliability in a variety of populations (0.95) (Raistrick,1994).

Furthermore, in a sample of patients attending the Leeds Addiction Unit, the LDQ was also found to have high internal consistency (Heather, 2001). It has also been found to be sensitive to change over the course of treatment in alcohol dependent adults (Tober, 2000). However, the LDQ appears to show a ceiling effect and does not reflect those at the more severe end of dependence (Heather, 2001). Ford (2003) evaluated the use of the LDQ in a psychiatric population and reported excellent internal reliability and acceptable concurrent validity with clinical opinion. The authors conclude that the LDQ is a sensitive to the degree of substance dependence and applicable to a population with severe mental health problems in an inpatient setting. The LDQ has also been found to have high internal consistency in a juvenile delinquent sample (Lennings, 1999).

In a young adult population (18-25 years old) undergoing residential treatment for substance dependence, the LDQ was reported to have high internal consistency, acceptable (but lower than expected) concurrent validity when compared to DSM-IV dependence criteria and percentage days abstinent (Kelly, 2010). Additionally, in a young adult population (mean age 20.3 years), the LDQ had satisfactory test-retest reliability and internal consistency (Thomas, 2008).

The LDQ is an applicable diagnostic measure of severity of alcohol dependence and hence can be used for other purposes in a clinical setting such as for setting treatment goals and outcome monitoring. Furthermore, it is brief and does not require training for administration and scoring. It was developed and validated in the UK and is free to use.

5.18 The assessment of problems associated with alcohol misuse

5.18.1 Introduction

The causal relationship between alcohol consumption and alcohol related problems such adverse social consequences, physical disease and injury is well established (Rehm *et al.,* 2009; Drummond, 1990). The extent to which alcohol is attributable to the range of alcohol related problems means that those presenting for clinical interview may experience considerable problems that are diagnostically important in helping to establish if the patient is experiencing harmful alcohol use or alcohol dependence.

From the initial review the GDG identified one measures for inclusion in the narrative review of tool to measure problems associated with alcohol misuse; this is the Alcohol Problems Questionnaire (APQ) (Drummond, 1990). Several other questionnaires were identified which included alcohol related problem items but these were mixed with other conceptual content (for example, dependence symptoms). Information on the characteristics of the APQ are summarised in Table 9 and Table 10.

Table 14: **Assessment tools included in narrative review**

Assessment instruments included in narrative review	Population		Assessment Category				
	Adult	Young people (>10 years)	Dependence	Consumption & frequency	Alcohol withdrawal	Motivation & readiness to change	Harm & alcohol problems
Alcohol Problems Questionnaire (APQ)	•						•[1]
Alcohol Use Disorders Identification Test (AUDIT)	•	•	•[1]	•	•[1]		•
Clinical Institute Withdrawal Assessment (CIWA–Ar)	•				•[1]		
Leeds Dependence Questionnaire (LDQ)	•	•(>16 years)	•[1]				
Severity of Alcohol Dependence Questionnaire (SADQ)	•		•[1]	•	•		
Readiness to Change Questionnaire Treatment Version (RTCQ–TV)	•	•				•[1]	

Subscript Key:- 1 = Primary Use

Table 15: Characteristics of assessment tools included in narrative review

Assessment instrument	Number of items & format Scale & cut-offs	Time to administer & by whom Training required for administration	Time to score & by whom	Copyright & cost of test
Alcohol Problems Questionnaire (APQ)	44 items (8 sub-scales), pencil and paper self-administered Maximum score = 23	3 to 5 minutes, respondent No training	Minimal, minimally trained technician	No; free to use
Alcohol Use Disorders Identification Test (AUDIT)	10 items (3 subscales), pencil and paper or computer self-administered Scale:- 0-40; Cut-offs:- >8 = hazardous, 16-19 = harmful, mild or moderate dependence, >=20 = severe dependence	2 minutes, trained personnel Minimal training	1 minute, trained personnel	Yes; Test and training manual free to use, Training costs $75
Clinical Institute Withdrawal Assessment (CIWA–Ar)	8 items, observation format Total score ranges from 0-6; Minimal/absent withdrawal: 0 – 9; Mild/moderate withdrawal: 10 – 19; Severe withdrawal: ≥20	2 minutes, trained personnel Training required for administration	4 to 5 minutes, trained personnel	Yes; free to use
Leeds Dependence Questionnaire (LDQ)	10 items, paper and pencil self-administered Scale:- 0-30; Cut-offs:- 0= no dependence, 1-10 = low/moderate dependence, 11-20 = moderate/high dependence, 21-30 = high dependence	2-5 minutes; respondent or personnel No training	Half a minute, non-trained personnel	No; free to use
Readiness to Change Questionnaire Treatment Version (RTCQ–TV)	15 (3 subscales). Most up-to-date version has 12 items, pencil and paper self-administered Original total score range: -10 to +10, Current version total score range: -8 to +8	2-3 minutes, respondent No training	1 minute, non-trained personnel	Yes; free to use
Severity of Alcohol Dependence Questionnaire (SADQ)	20 (5 sub-scales), pencil and paper self-administered Scale:- 0-60; Cut-offs:-<16 = mild dependence, 16-30 = moderate dependence, ≥31 = severe dependence	5 minutes, respondent No training	1 minute, trained personnel or clinician	No; free to use

Table 16. Assessment tools excluded from narrative review

Assessment tools excluded from narrative review	Population		Assessment category						Refe
	Adult	Young people (>10 years)	Dependence	Consumption & frequency	Alcohol withdrawal	Motivation & readiness to change	Harm & alcohol problems	Clinical interview tool	
Adolescent Alcohol Involvement Scale (AAIS)		•	•[1, 2]	•[1]					Mayer & F
Adolescent Drinking Index (ADI)		•	•[1, 2]						Harrell &
Alcohol Dependence Scale (ADS)	•		•[1]		•				Skinner &
Alcohol Withdrawal Syndrome Scale (AWS)	•								Wetterling
Clinical Institute Withdrawal Assessment (CIWA-AD)	•				•[1]				Sullivan
Cognitive Lifetime Drinking History (CLDH)	•			•[1]					Russell
Composite International Diagnostic Interview (CIDI) Version 2.1	•		•	•	•			•[1]	Robins
Comprehensive Addiction Severity Inventory for Adolescents (CASI-A)[3]		• (>16 years)	•[1, 2]					•[1]	Meyers
Customary Drinking and Drug Use Record (CDDR)[3]		•	•[1, 2]		•		•	•[1]	Brown
Diagnostic Interview Schedule (DIS–IV) Alcohol Module	•		•					•[1]	No Source
Drinker Inventory of Consequences (DrInC)	•						•[1]		Miller
Drinking Problems Index (DPI)	•						•[1]		Finney
Drinking Self–Monitoring Log (DSML)	•	•		•[1]					Sobell *et al.* *et al.*
Ethanol Dependence Syndrome (EDS) Scale	•		•[1]		•				Babo
Form 90-AQ (Alcohol Questionnaire)	•	•		•[1]					No Source

Subscript Key:- 1 = primary use; 2 = assesses dependence or abuse;

Table 17. Assessment Tools Excluded from Narrative Review

Assessment tools excluded from the narrative review	Population		Assessment category						R
	Adult	Young people (>10 years)	Dependence	Consumption & frequency	Alcohol withdrawal	Motivation & readiness to change	Harm & alcohol problems	Clinical interview tool	
Global Appraisal of Individual Needs (GAIN)	•	•	•			•	•	•[1]	Denn
Lifetime Drinking History (LDH)	•			•[1]					Skinne
Mini International Neuropsychiatric Interview -Clinician Rated (MINI)-CR	•		•					•[1]	Sheeh
Motivational Structure Questionnaire (MSQ)	•	•				•[1]			Cox &
Personal Experience Inventory (PEI)[3]		•	•[2]				•[1]		Winters
Psychiatric Research Interview for Substance and Mental Disorders (PRISM)	•		•		•		•	•[1]	Hasin (
Quantity–Frequency (QF) Methods	•	•		•[1]					No Sou
Rutgers Alcohol Problem Index (RAPI)		•	•[1, 2]				•[1]		White &
Semi–Structured Assessment for the Genetics of Alcoholism (SSAGA–II)	•		•					•[1]	Buch
Short Alcohol Dependence Data (SADD)	•		•[1]						Raistr
Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) - Version 8	•					•[1]			Miller &
Structured Clinical Interview for the DSM Substance Use Disorders Module (SCID SUDM)		•	•[1, 2]					•[1]	Mart
Substance Use Disorders Diagnostic Schedule (SUDDS-IV)[3]		•(>16 years)	•[1,2]					•[1]	Hoffman
Timeline Followback (TLFB)	•	•		•[1]					Sobe
University of Rhode Island Change Assessment (URICA)	•					•[1]			DiClem

Subscript Key:- 1 = primary use; 2 = assesses dependence or abuse;

5.18.2 Alcohol Problems Questionnaire (APQ)

The Alcohol Problems Questionnaire (APQ) (Drummond, 1990) was developed for use as a clinical instrument which assesses problems associated with alcohol alone independent of dependence. The APQ is a 44-item questionnaire (maximum score possible = 44) which assesses eight problem domains (friends, money, police, physical, affective, marital, children, and work). The first five domains make up 23 items that are common to all individuals. The maximum score of 23 is derived from these items to arrive at a common score for all individuals.

In the original validation study of the APQ, Drummond (1990) reported that the APQ common score (based on the common items) was significantly highly correlated with total SADQ score (r = 0.63) and drinking quantity as indicated by the appropriate items of the SADQ (r = 0.53). Partial correlations however (which controls for each item included in the analyses) revealed that there was a highly significant relationship between alcohol-related problems and alcohol dependence which is independent of the quantity of alcohol consumption (Drummond, 1990). Williams & Drummond (1994) similarly reported a highly significant correlation between the APQ common score and the SADQ (r = 0.51) and a significant *partial* correlation between the APQ common score and SADQ (controlling for alcohol consumption) (r = 0.37). However, when controlling for dependence, the partial correlation between alcohol problems as measured by the APQ and alcohol consumption was low, which suggests that dependence level mediates the relationship between these two variables (Williams & Drummond, 1994). The results of these two studies indicate that the APQ has high reliability and validity for assessing alcohol-related problems in an alcohol dependent population.

The APQ has been widely used in alcohol treatment outcome studies as a measure of alcohol-related problems in the UK (for example, Drummond *et al*., 1990; UKATT research group, 2005; Drummond *et al*., 2009). Furthermore, it is quick and easy to administer.

5.19 The assessment of motivation

Self-awareness with respect to the adverse consequences of drinking, levels of motivation and readiness to change drinking behaviour vary enormously across the population presenting for alcohol treatment. The need to assess such issues is widely accepted. For example, Raistrick *et al* (2006) noted that "An understanding of the service user's motivation to change drinking behaviour is a key to effective treatment and can be used to decide on the specific treatment offered". A number of methods have been developed to aid the assessment of motivational status, these are usually linked to the cycle of change developed by Prochaska and DiClemente (1983) are designed to site drinkers at specific stages within the cycle. The key stages of change are pre-contemplation (seemingly unaware of any problem), contemplation (aware and considering change), preparation (decision to change taken, planning what to do), action (doing it) and maintenance (working to secure the change).

From the initial review the GDG identified two related measures for possible inclusion in the narrative synthesis of tools to measure motivation in people with alcohol misuse problems; these are the Readiness to Change Questionnaire (RCQ)

(Rollnick *et al.,* 1992) and the Readiness to Change Questionnaire - Treatment Version (RCQ-TV) (Heather *et al.,* 1999). The original RCQ is for a harmful and hazardous non-treatment seeking population and hence is not described in this narrative review.

5.19.1 Readiness to change questionnaire- treatment version (RCQ-TV)

The Readiness to Change Questionnaire – Treatment Version (RCQ-TV) (Heather et al. 1999) was developed from the original RCQ for use in a treatment-seeking alcohol misuse population. Both versions refer to deinking reduction. However, the treatment version also refers to abstinence from drinking and also has items which refer to the maintenance as well as a preparation stages. The RCQ-TV has 15 items and 3 sub-scales (pre-contemplation, contemplation and action). The items are scored from -2 (strongly disagree) to +2 (strongly agree) with a maximum of 10 and minimum of minus 10.

Heather et al (1999) found low item-total correlations for the pre-contemplation, contemplation and action scale of the RCQ-TV. Internal consistencies were low to moderate (Cronbach's α ranged from 0.60 to 0.77 across sub-scales). Test-retest reliability was adequate (r = 0.69 to 0.86 across sub-scales). With regards to concurrent validity, those in the contemplation group reported drinking more than those in the action group, had less desire to stop drinking and reported less confidence in being able to stop drinking. The various sub-scales on the RCQ-TV correlated significantly with their URICA equivalents (i.e. pre-contemplation, contemplation and action), although correlations were small in magnitude (e.g. r= .39 to .56).

Participants who had been in treatment for more than 6 months or who had had any treatment were more likely to be in the action group than those treated for less than 6 months or those who had had no treatment(x^2 = 8.75, p<0.005). Similarly, those initially assigned to the action group were more likely than those in the contemplation group to have a good outcome at follow-up. This result remained when re-classifying participants at follow-up.

Heather and Hönekopp (2008) looked at the properties of the standard 15-item version as well as a new 12 item version of the RCQ-TV in the UKATT sample of participants. The authors reported that there was little difference between the two versions. For example, the internal consistency of the 15-item version ranged from α = 0.64 to 0.84 across sub-scales and for the 12-item version α = 0.66 to 0.85 across sub-scales. Both versions showed adequate consistency over time when assessed at three and twelve month follow-up. Heather and Hönekopp (2008) also assessed the construct validity of both versions of the RCQ-TV by analysing their correlation with other important variables, namely percentage days abstinent, drinks per drinking day and alcohol problems (using the APQ). Both versions showed a low correlation with these items at baseline but high correlations at 3 and 12 month follow-up, indicating that the RCQ-TV may have good predictive value. However, the shorter version was better able to predict outcome (unsigned predictive value of 12-item version varied between r = 0.19 to 0.43).

As the RCQ-TV has seen specifically developed for a treatment-seeking population it has value for both treatment planning and monitoring. Furthermore, it is short, and

requires no training for administration. Although it is copyrighted, it is available for no cost by contacting the original developers.

5.19.2 Evidence summary

The above narrative review identifies a number of tools used in the assessment of several domains and that met the criteria set out at the beginning of this section and which the GDG considered to be feasible and appropriate to use in a NHS or related healthcare setting. They are listed below:

The Alcohol Use Disorders Inventory Test (AUDIT) – for case identification and initial assessment of problem severity

The Severity of Alcohol Dependence Questionnaire (SADQ) - to the asses the presence and severity of alcohol dependence

The Leeds Dependence Questionnaire (LDQ) - to the asses the presence and severity of alcohol dependence

The Alcohol Problems Questionnaire (APQ) - to the asses the nature and extent of the problems associated with of alcohol misuse

Three tools reviewed above were not considered to be of value for routine use in the NHS and related services. They were: the Drinker's Inventory of Consequences (DrInC) (Miller *et al*., 1995) – this is primarily a research tool validated on US population and lacks clear cut offs to be of value in the NHS; the Readiness to Change Questionnaire- Treatment Version (RCQ-TV) (Heather *et al*., 1999) which adopts too narrow a focus on motivation and was felt to add little to what might be obtained from a clinical interview and the Alcohol Dependence Scale (ADS) (Skinner & Horn, 1984) was not included as it was felt to have no advantage over either the SADQ or LDS but was copyrighted and did require a fee for use.

The assessment tools above can only be fully effective when they are used as part of a structured clinical assessment, the nature and purpose of which is clear to both staff and client. The nature and purpose of the assessment will vary according to what prompts the assessment (for example, a request for help from a person who is concerned that they are dependent on alcohol or further inquiries following the diagnosis of liver disease which is suspect to be alcohol related).

The following section of the guideline aims to review the structures for the delivery of assessment services. The following review will then provide the context in which the recommendations for assessment are developed.

5.20 The structure and content of the assessment interview

5.20.1 Introduction

In developing this section of the chapter the GDG drew on publications on the structuring and settings for the delivery of alcohol services (MoCAM (DH, 2006)) and also the two recent NICE guidelines on the treatment and management of

alcohol related problems (NICE, 2010a; NICE 2010b). The NICE guidelines were particularly important in setting the context for and the limits of this review. A number of authors have set out the aims and components of an assessment for alcohol misuse including Edwards *et al*., (2003), MoCAM (DH, 2006) and Raistrick *et al* (2006). The common aims for assessment of alcohol misuse that emerge from these authoritative reviews are:

- establishing the presence of an alcohol use disorder
- the level of alcohol consumption
- determining whether the alcohol use disorder is best characterised as harmful drinking or alcohol dependence
- establishing the presence of acute risks (for example, self-harm, harm to other, medical/mental health emergencies, safeguarding children issues)
- establishing the capacity to consent to treatment or onward referral
- experience and outcome of previous intervention(s)
- establishing the willingness to engage in further assessment and/or treatment
- establishing the presence (but not necessarily diagnosing) of possible co-existing common problems features (for example, co-ocurring substance misuse, medical, mental health and social problems)
- determining the urgency of referral and/or an assessment for alcohol withdrawal

The following sections describe in some detail the key aspects of alcohol misuse. The extent to which they are addressed in the description of the different assessment systems that follow with vary according to the needs of the service user, the service in which the assessment is delivered, the specific purpose of the assessment and the competence of the staff undertaking the assessment. Nevertheless all staff undertaking an assessment of alcohol misuse will need to be familiar with the issue described below.

5.20.2 Alcohol use

For harmful alcohol use or alcohol dependence to be identified three domains need to address; alcohol consumption, features of alcohol dependence and alcohol problems (Edwards *et al*., 2003; Allen, 2003. It should be remembered that to arrive at a diagnosis of harmful alcohol use alcohol dependence needs to be excluded and therefore dependence features need to be considered for all those undergoing diagnostic clinical interview (ICD-10; WHO, 1992). Baseline alcohol consumption and severity of alcohol dependence have been identified as potentially significant predictors of treatment outcome (Adamson *et al*., 2009).

5.20.3 Consumption

Harmful effects of alcohol use have been found to be influenced by both the amount and pattern of alcohol consumption (Rehm *et al*., 2004). Assessing typical daily and weekly alcohol consumption and comparing findings with recommended levels of alcohol consumption is therefore a useful starting point.

Individuals may present at different stages of a drinking cycle it is important to acknowledge that the absence of current alcohol use does not exclude the patient from being diagnosed with an alcohol use disorder (WHO, 1992). Therefore an overview of the patient's current drinking status, preferred type of alcohol/brand

consumed, the setting in which this occurs and general amount consumed is an important part of a assessment (Edwards *et al*., 2003; MoCAM; DH, 2006). Usually the assessment of consumption and frequency relies on the evaluation of self-reported alcohol consumption. Sobell & Sobell (2003) considered previous reviews of the validity and reliability of self-reported alcohol consumption and found that enhanced accuracy included individuals who are: i) alcohol free when interviewed; ii) given written assurances of confidentiality; iii) interviewed in a setting that encourages openness and honesty; iv) asked clearly worded questions and v) provided memory aids to recall drinking (i.e. drink diaries), with those interviewed with alcohol in their system tending to underestimate their consumption. Previous reviews support the concept or enquiring about the patient's typical drinking day (Rollnick *et al*., 1999; Edwards *et al*., 2003). The notion of focusing on the typical drinking day allows staff to focus on what may normally occur in the absence of other factors that may influence large variations in alcohol consumption (i.e. stress, finances, life events) that may be misleading. Regular high-level alcohol consumption may indicate tolerance to alcohol that has a significant relationship to alcohol dependence and consequent alcohol withdrawal.

The evolution of the patient's current alcohol consumption over time needs to be considered in order to identify significant patterns of alcohol use that are diagnostically important. In a more detailed assessment the concept of drinking milestones may help to identify the time of first drink through to present alcohol consumption. Edwards *et al.* (2003) suggests the inclusion of milestones such as; age of first alcohol drink, first drinking most weekends, first drinking daily on daily basis and when commenced drinking at current levels. Additionally, it is important to document when the patient recognises the following; when they first felt alcohol was a problem, the heaviest period of alcohol consumption and significant periods where they have experienced being alcohol free. Seeking clarification with regards to typical quantities of alcohol consumed at significant milestones with help establish the development of potential alcohol misuse.

5.20.4 Dependence

Those who drink alcohol dependently develop adjustments in relation to alcohol being present or absent in the body. Regular alcohol consumption can result in central nervous system (CNS) changes that adapt and compensates to the depressants effects alcohol in the body. If this adaptation occurs these changes may also result in CNS being hyper-excited when alcohol levels are reduced presenting characteristic alcohol withdrawal symptoms. Sensitive exploration of the six individual alcohol dependence criteria will confirm a diagnosis and help the individual to understand and acknowledge the condition they experience (Edwards *et al*., 2003). It is generally accepted that a number of aspects of dependence should be covered in a comprehensive assessment include tolerance, neglecting activities and interests, compulsion, physiological withdrawal and drinking despite problems (Maisto *et al*., 2003).

5.20.5 Tolerance

Regular alcohol drinkers become tolerant to the central nervous system effects of alcohol (Kalant, 1996). There appears to be a number of individual factors that influence the development of tolerance to alcohol including metabolic, environmental and learned factors (Tabakoff *et al*., 1986). Individual variance

therefore makes it unclear at what level tolerance to alcohol occurs although higher consumption levels will be indicative of tolerance. The effect of blood alcohol concentration (BAC) on an individual will decrease as tolerance develops (Hoffman & Tabakoff, 1996) but even in tolerant individuals high level alcohol consumption will still impair functioning and judgment.

5.20.6 Physiological withdrawal

Personnel will need understand and recognise alcohol features of alcohol withdrawal to accurately arrive at a diagnosis of alcohol dependence. Personnel will need to accurately differentiate between alcohol withdrawal symptoms and other clinical characteristics and clinical conditions that may present similarly.

Alcohol withdrawal symptoms include:

- Tremor
- Nausea
- Sweating
- Mood disturbance including agitation and anxiety
- Disturbed sleep pattern
- Hyperacusis – sensitivity to sound
- Hyperthermia – increased body temperature
- Tachycardia – increased pulse rate
- Increased respirations
- Tactile and/or visual disturbances – itching, burning, etc

Severe alcohol withdrawal symptoms include:

- Hallucinations – auditory, visual and/or tactile
- Alcohol withdrawal seizures – grand mal type seizure
- Delirium Tremens - coarse tremor, agitation, fever, tachycardia, profound confusion, delusions and hallucinations

Some individuals that consume alcohol in quantities outside healthy limits will develop an acute alcohol withdrawal syndrome when they abruptly stop or substantially reduce their alcohol consumption. Most patients manifest a minor symptom complex or syndrome, which may start as early as six to eight hours after an abrupt reduction in alcohol intake. Table 12 provides an illustration of alcohol withdrawal symptoms against a timeline since last drink.

Table 18: Illustrative timeline for the emergence of alcohol withdrawal symptoms

Timeline from last drink	Alcohol withdrawal symptoms
From: 6-8 hours Peak: 10-30 hours Subsides: 40-50 hours	Generalised hyperactivity, tremor, sweating, nausea, retching, mood fluctuation, tachycardia, increased respirations, hypertension and mild pyrexia
From: 0-48 hours	Withdrawal seizures
From: 12 hours Duration: 5-6 days	Auditory and visual hallucinations may develop which are characteristically frightening
From: 48-72 hours	Delirium tremens (DTs): coarse tremor, agitation, fever, tachycardia, profound confusion, delusions and hallucinations

The individual may describe the use of alcohol to avoid or ameliorate the effects of alcohol withdrawal, which would further demonstrate physiological dependence to alcohol.

5.20.7 Compulsion

An individual's compulsion to consume alcohol is commonly reported when an alcohol dependent drinker attempts to control or stop use (Drummond & Phillips, 2002). In developing a care plan, information about the situations and emotional states that influence the presence and intensity of compulsion to use alcohol, as this may be an important feature in predicting future drinking episodes. (Monti *et al.*, 2000).

5.20.8 Neglecting activities and interests

Individual who are dependent on alcohol may describe a reduction or change in their participation in activities they hold as important (Drummond, 1990). As alcohol becomes increasingly more dominant, the need to obtain, consume and/or recover from excessive alcohol consumption has higher priority. Again identifying the priority alcohol has for the individual - exploring past and current interests with the individual may help signpost a reduction in activities as alcohol consumption has escalated.

5.20.9 Drinking in spite of problems associated with alcohol

Alcohol-related problems occur in the absence of alcohol dependence (that is, accidents, legal problems, and so on). However, a person dependent on alcohol may maintain drinking behaviour despite clear evidence of harmful effects causally related to alcohol such as harm to the liver and depressed mood (Drummond, 1990). The individual may describe the continuation of alcohol use despite criticisms from family, friends, and work colleagues and continue to use alcohol regardless of further consequences.

5.20.10 Alcohol and other substances of abuse

The assessment of alcohol misuse is often complicated by the presence of co-occurring conditions, these, along with the implications for assessment, are outlined below.

Comorbid opioid and alcohol dependence

In treatment services for opioid dependency, about a quarter to a third of patients will have problems with alcohol (DH, 2007). In addition, prognosis for this group can be poor with many showing limited changes in drinking behaviour. A recent systematic review about whether alcohol consumption is affected during the course of methadone maintenance treatment concluded that alcohol use is not likely to reduce by just entering such programmes, with most studies reporting no change (Srivastava *et al.*, 2008). In the UK National Treatment Outcome Research Study, 25% of opiate misusers were drinking heavily (>10 units/day) at the start of the study and 4-5 years later about a quarter were continuing to do so (Gossop *et al.*, 2003).

Comorbid cocaine and alcohol dependence

Cocaine use is increasing in England (Statistics on Drug Misuse: England, 2009) and comorbid cocaine and alcohol dependence is commonly seen and can be challenging to treat. There is little known in UK about level of this comorbidity in alcohol

treatment services. In the US Epidemiological Catchment Area study, 85% of cocaine-dependent patients were also alcohol dependent (Regier *et al.*, 1990). In a sample of 298 treatment-seeking cocaine users, 62% had a lifetime history of alcohol dependence (Carroll *et al.*, 1993). In a sample of people in contact with drug treatment agencies mainly for opiate addiction and in the community abusing cocaine, heavy drinking was common. Those using cocaine powder were more likely to drink heavily than those using crack cocaine (Gossop *et al.*, 2006).

When taken together, cocaine and alcohol interact to produce cocaethylene, an active metabolite with a half-life three times that of cocaine. In addition alcohol inhibits some enzymes involved in cocaine metabolism, so can increase its concentration by about 30% (Pennings *et al*, 2002). Due to the presence of cocaethylene which has similar effects as cocaine and a longer half-life, this leads to enhanced effects. For instance, taken together cocaine and alcohol result in greater euphoria and increased heart rate compared to either drug alone (McCance-Katz *et al.*, 1993, 1995; see Pennings *et al.,* 2002).

Comorbid alcohol and benzodiazepine dependence

Benzodiazepine use is more common in patients with alcohol misuse than in the general population, with surveys reporting prevalence of around 10-20% (Ciraulo *et al*, 1988; Busto *et al*, 1983). In more complex patients, it can be as high as 40% which is similar to that seen in psychiatric patients. Not all use will necessarily be misuse. For some individuals, their growing dependence on benzodiazepines began when a prescription for withdrawal from alcohol was extended and was repeatedly renewed. For others, the prescription may have been initiated as a treatment for anxiety or insomnia.

Comorbid alcohol and nicotine dependence

Many patients with alcohol misuse smoke cigarettes which causes an extra burden of morbidity and mortality to that caused by their alcohol misuse. The prevalence of nicotine smoking has been estimated at around 40% in population based studies of alcohol use disorder but as high as 80% in treatment seeking alcoholics (Grant *et al.*, 2004, Hughes, 1995). Comorbidity is higher in men than women, in younger compared to older people (Falk *et al.*, 2006, NIAAA). Comorbid nicotine and alcohol dependence has been comprehensively reviewed recently by Kalman *et al* (2010).

5.20.11 Motivation and self-efficacy

The assessment of an individual's willingness to engage in any treatment or assessment programme can vary considerably and has been the subject of considerable debate. Assessment can be effective as an intervention in itself, and has been shown to influence behaviour change (Orford & Edwards, 1976; Kypri *et al.*, 2007; McCambridge & Day, 2008); increasing an individual's confidence towards change that may prompt reductions in alcohol consumption (Rollnick *et al.*, 1999). Being sensitive to the individual's needs, developing rapport and a therapeutic alliance have all been identified as important aspects in the effective engagement of an individual who drinks excessively (Najavitis & Weiss, 1994; Raistrick *et al.*, 2006; Edwards *et al.*, 2003). Indeed there is evidence to suggest that a premature focus on information gathering and completion of the assessment process may have a negative impact on the engagement of the patient (Miller & Rollnick, 2002). Where

this approach is adopted there is some evidence to suggest that initial low levels of motivation are not necessarily a barrier to an effective assessment and the future uptake of treatment (Miller & Rollnick, 2002).

An openness to discussion aimed at understanding a person's reasons for seeking help and the goals they wish to attain has also been positively associated with engagement in assessment and treatment (Miller, 1996) The individual's personal drinking goals can then be acknowledged and used as a basis for negotiation once the assessment is completed (Adamson *et al.*, 2010).

As has also been acknowledged at a number of points in this guideline, alcohol related problems present in a number of different settings, often concurrently (for example, a person may present as depressed in primary care subsequent to a brief admission for acute pancreatitis, both related to excessive alcohol intake). It has therefore long been recognised that effective assessment systems need to be linked to equally effective communication amongst those involved in the care and treatment of people with alcohol related problems (Maisto *et al.*, 2003). Sharing of information between agencies should be encouraged to maximise safety and effectiveness of treatment (MoCAM, DH, 2006).

5.20.12 Framework for assessment of alcohol misuse

As noted above, the presentation of alcohol related problems are rarely straightforward and can span a wide range of settings and organisations. This complexity of presentation is often matched by an equal complex response in terms of the assessment or treatment responses that are required. It is therefore important that clear structures are in place to identify and assess the presenting problems, determine the most appropriate treatment option and, where necessary, make an appropriate referral. This section reviews the evidence, albeit very limited, for the organisation and delivery of assessment systems. In doing so it not only draws on the evidence that relates directly to the organisation and delivery of care (see Section 2 of this chapter) but also the evidence reviewed in the two other alcohol NICE guidelines on prevention and early detection (NICE 2010a) and on management of alcohol-related physical complications (NICE, 2010b), and to other parts of this guideline which consider evidence relevant to a framework for the assessment of alcohol misuse. It should be noted that the framework of assessment in this guideline is not specifically concerned with the opportunistic screening for alcohol related problems which is covered by the NICE (2010a) guideline on prevention and early detection. However, it is important that the assessment framework does consider those who may seek treatment and those who do not respond to brief interventions.

In developing the framework for assessment, the evidence for the discussion of stepped care systems in Section 2 of this chapter was particularly influential. The evidence review proved no convincing evidence to suggest a significant variation for the stepped care framework set out in the Models of Care for Alcohol Misusers paper (MoCAM) (DH, 2006) developed by the National Treatment Agency Building on both the work in the MoCAM paper a conceptualisation for the assessment (and management) of harmful drinking and alcohol dependence at four levels emerges10. This is set out below:

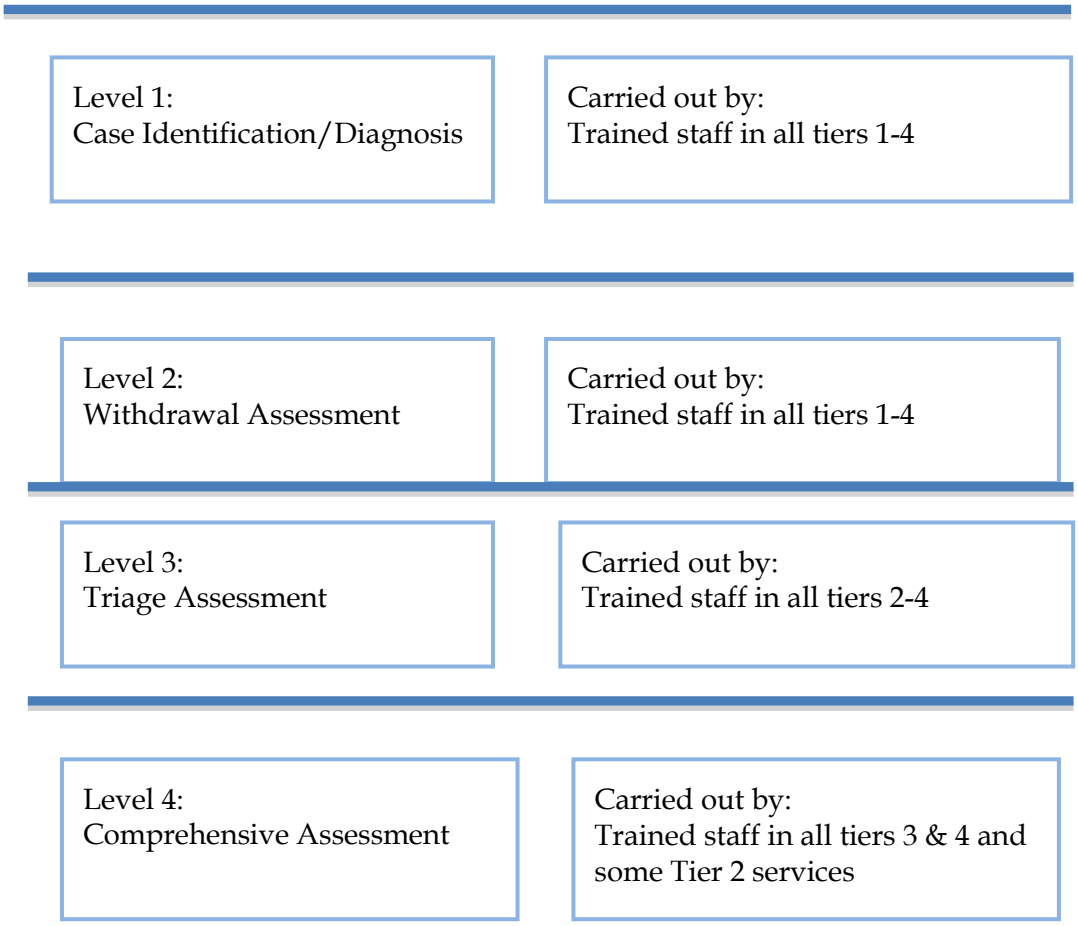
[10] The terms levels and tiers are adopted from the MoCAM (DH, 2006) to facilitate ease of understanding and implementation.

1. Case identification/diagnosis
2. Withdrawal Assessment
3. Triage Assessment
4. Comprehensive Assessment.

These four levels, which are defined below, take account of the broad approach to the delivery of assessment and interventions across different agencies and settings including; primary health care, third sector providers, criminal justice settings, acute hospital settings, specialist providers. It should be noted however that this does not follow a strictly stepped care model as an assessment for withdrawal could follow from a triage and a comprehensive assessment. Withdrawal assessment was not included in the MOCAM assessment framework as a separate assessment algorithm, but was considered by the GDG to merit separate inclusion in these guidelines. Alcohol withdrawal assessment is an area of clinical management that often requires immediate intervention. This is particularly apparent where an alcohol dependent individual may experience acute alcohol withdrawal as a consequence of an admission to an acute hospital ward (see NICE guideline on management of alcohol-related physical complications; 2010), due to an acute health problem or has been recently committed to prison.

The framework for assessment (see Figure 2) sits alongside the four-tiered conceptual framework described in MoCAM (DH, 2006) and assumes that appropriately skilled staff will only undertake the assessment elements. The Drug and Alcohol National Occupational Standards (DANOS (Skills for Health, 2002) set out the skills required to deliver assessment and interventions under the four-tiered framework. In line with a stepped care approach the different levels of assessment require varying degrees of competence and specialist skills and expertise to undertake the more complex assessments.

Figure 4. Assessment levels



5.21 The framework for assessment of alcohol misuse

5.21.1 Case identification and diagnosis

Aims

Case identification and following on from that diagnosis seeks to identify those individuals with alcohol misuse with that are in need of intensive care-planned treatment because of possible alcohol dependence, those with harmful alcohol use who are in need of or have not responded to brief interventions and those comorbid problems which may complicate the treatment of the alcohol misuse. Given the overall stepped framework in which the assessment takes place it is anticipated this level of would have three objectives:

a) To identify those individuals who need an evidence based intervention (see Chapters 6 and 7) for harmful or mildly dependent alcohol misuse
b) To identify those who may need referral for a comprehensive assessment and/or withdrawal assessment including those who:

- have not responded to an extended brief intervention
- moderate to severe alcohol dependence or otherwise may need assisted alcohol withdrawal
- those that show signs of clinically significant alcohol-related impairment (for example, liver disease or significant alcohol related mental health problems)

Settings

Case identification and diagnosis are activities that should be available across the whole range of healthcare and related services (for example, general practitioners, accident and emergency departments, children and families social services).

Method

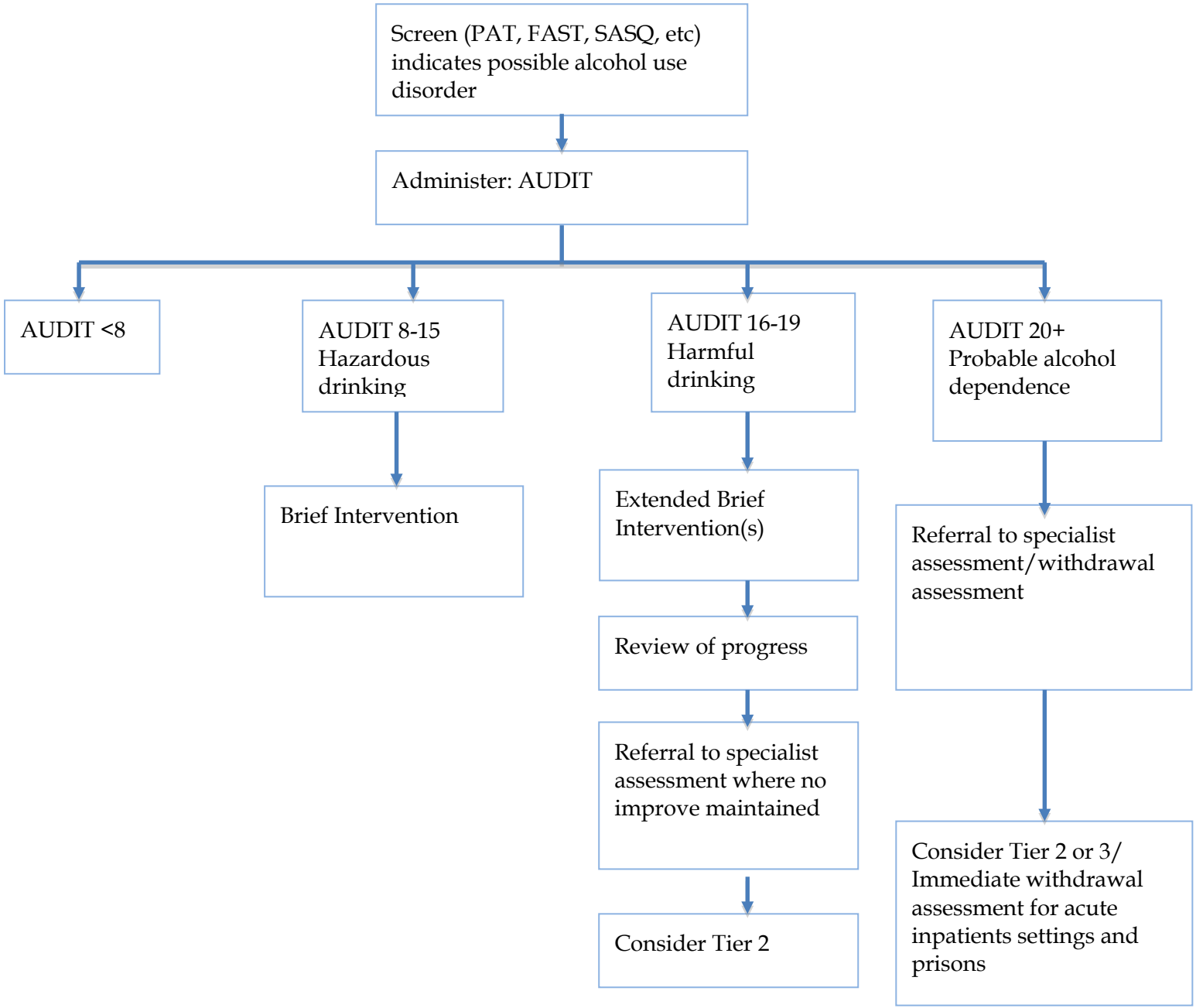
This level of assessment should consider those elements stated above including:

- establishing the probable presence of an alcohol use disorder
- the level of alcohol consumption (as units[11] of alcohol per day or per week)
- where an alcohol use disorder is suggested, distinguish of harmful drinking or alcohol dependence
- establishing the presence of acute risks (for example, self-harm, harm to other, medical/mental health emergencies, safeguarding children issues)
- establishing the capacity to consent to treatment or onward referral
- experience and outcome of previous intervention(s)
- establishing the willingness to engage in further assessment and/or treatment
- establishing the presence (but not necessarily diagnosing) of possible co-existing common problems features (for example, additional substance misuse, medical, mental health and social problems)
- determining the urgency of referral and/or an assessment for alcohol withdrawal.

[11] The UK unit definition differs from definitions of standard drinks in some other countries. For example a UK unit contains 2/3 of the quantity of ethanol compared to a US 'standard drink'.

The treatment options that follow immediately from this initial assessment, with the exception of assisted withdrawal, will focus on harmful or dependent drinking. A significant number of individuals may already have received brief intervention and have not benefited from them; if this is the case then the individual will need to be referred for a comprehensive assessment.

Figure 5. Care pathway: case identification and possible diagnosis for adults



5.21.2 Level 2: withdrawal assessment

Aims

Assessment of the need for a medically managed withdrawal seeks to identify those individuals with alcohol dependence whose level of dependence is such that an unassisted withdrawal would pose a serious risk to the individual (for example the development of seizures or delirium tremens). A key factor will be determining whether the referral should take place in a community or an inpatient or residential setting. This section of the guideline should be read in conjunction with the section on planned assisted alcohol withdrawal in this guideline and the reader should also refer to the guideline on the management of acute withdrawal (NICE, 2010b). It should be noted that assisted withdrawal from alcohol should not be seen as a stand alone treatment for alcohol dependence but rather as an often essential element within a broader care plan including psychosocial or pharmacological therapies to prevent relapse. Specifically the withdrawal assessment should aim:

a) to identify those individuals who need an assisted withdrawal because of alcohol dependence
b) to identify:
    - the severity of the dependence
    - the level of alcohol consumption
    - the presence of comorbid factors such as substance misuse, severe psychiatric disorders, significant physical illness or disability
    - the availability of personal and social support and housing support
c) to identify in which setting a withdrawal can be most clinically, cost-effectively and safely managed
d) to determine the urgency with which the assisted withdrawal should be provided
e) to provide sufficient information to properly integrate the assisted withdrawal programme into a wider care plan.

Settings

Withdrawal assessments take place in a number of healthcare settings; the management of those presenting in acute medical settings is dealt with in NICE (2010b). However, although this guideline's recommendations are focused primarily on the management of planned withdrawal a number of the recommendation in this guideline will be relevant to the assessment of all individuals who are alcohol dependent and at risk of developing withdrawal symptoms. Primary care, prisons, police custody, general hospitals, secondary care mental health services and specialist drug and alcohol services are all settings in which the need for a withdrawal assessment may arise. These varied settings mean that the nature of the assessment will vary depending on the resources and skills available in those settings. However, as described in section 4 of this chapter there is evidence that assisted withdrawal from alcohol can be safely and effectively delivered in all those settings provided that an assessment has been performed to determine the most appropriate environment in which to undertake the withdrawal and the regimen required (Maisto *et al.*, 2003). It should be noted that there is a dose dependent relationship between alcohol consumption and the development of medical, mental health and social problems (Rehm *et al.*, 2009). The impact of comorbid conditions

and their implications for the choice of withdrawal setting is described more fully in section 4. A number of reviews (for example, Raistrick *et al*, 2006; NICE; 2010b) highlight factors which suggest the use residential or inpatient withdrawal programmes. These include: those who are assessed to be at high risk[12] of developing alcohol withdrawal seizures or delirium tremens; those with a history of poly-drug use; significant cognitive impairment; the homeless; and those with an illness that requires medical/surgical or psychiatric treatment.

Methods

Those who experience a significant degree of alcohol dependence will exhibit alcohol withdrawal symptoms 6-8 hours after their last drink, with peak effect of alcohol withdrawal symptoms occurring at between 10-30 hours (see NICE guideline on management of alcohol-related physical complications; 2010). Early diagnosis of alcohol dependence will help to initiate proactive management strategies for the individual and/or reduce risks to the patient.

The NICE guideline on management of alcohol-related physical complications (NICE, 2010) reviewed the accuracy of tools for the assessment and monitoring of patients who are alcohol dependent and at risk of developing alcohol withdrawal. The guideline recommends the use of a validated tool to support clinical judgement in the assessment of alcohol withdrawal. Furthermore, the guideline recommended the use of an assessment tool in situations particularly where staff are less experienced with the assessment of alcohol withdrawal. The guideline identified the CIWA-Ar as a valuable tool for measuring alcohol withdrawal symptoms. The guideline also noted that a delay of more than 24 hours is associated with greater withdrawal complications.. In this all settings it is generally preferred to support a clinical assessment with the use of formal measures (such as CIWA-Ar).

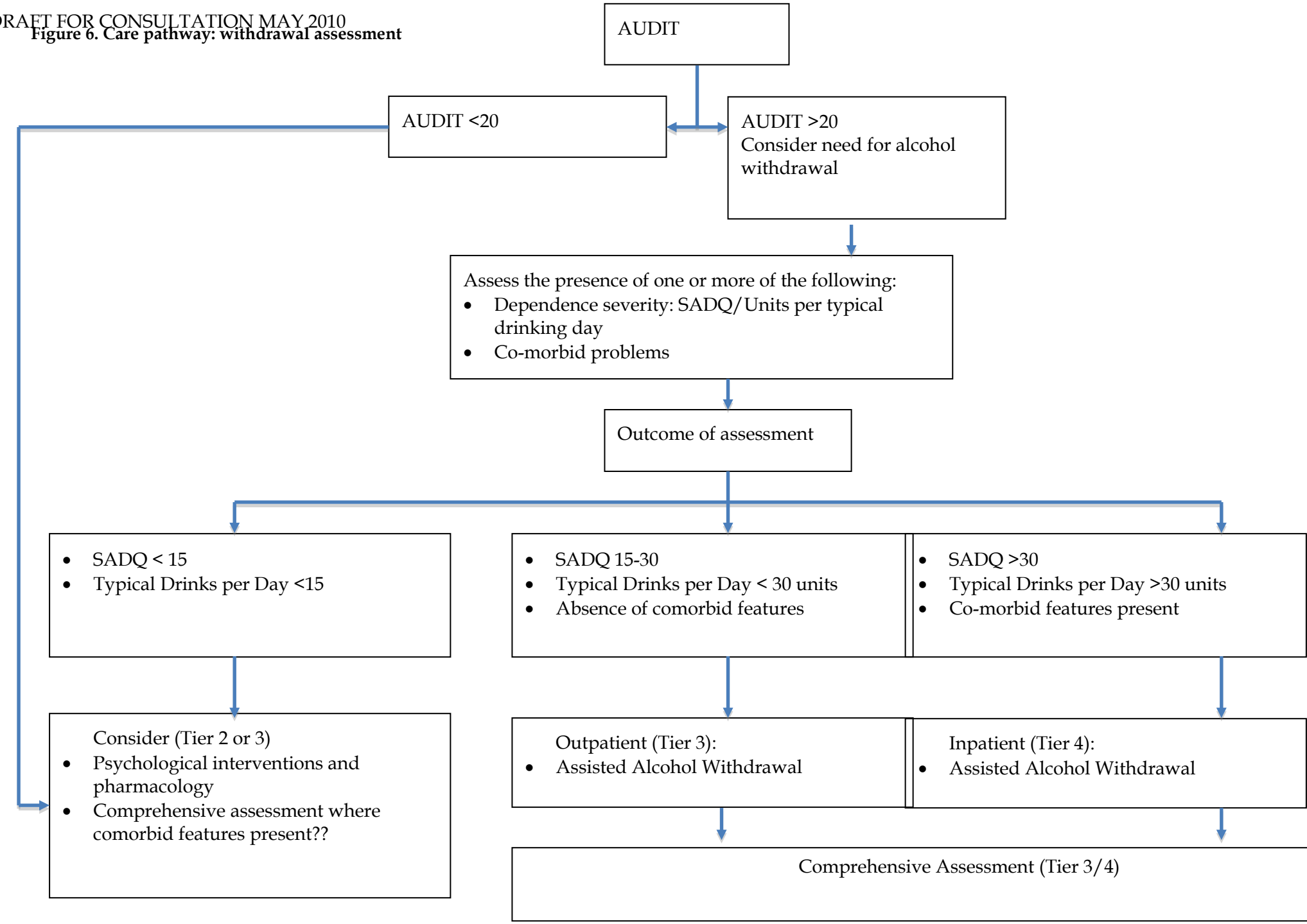
After establishing the possibility of alcohol misuse it is important to establish first whether or not dependence is present; in all settings this is a two stage process. The first stage involves the identification of those at risk of dependence and withdrawal. The preferred aid to a clinical assessment is the AUDIT questionnaire. An AUDIT score greater than 20 is an indication of likely alcohol dependence and the need for withdrawal assessment (Babor *et al*., 2001b). If it is not possible to complete an AUDIT questionnaire then regular consumption of alcohol of 15 to 20 or greater units per day suggests likely dependence. Although there is no absolute level of daily or weekly alcohol consumption which indicates the likelihood of alcohol dependence, the SADQ scores (a measure of the severity of dependence - see above) correlate with high-level alcohol consumption (Stockwell *et al*., 1979). Others support the view that typical drinks per drinking day is a useful indicator of the severity of alcohol dependence and need for alcohol withdrawal management (Shaw *et al*., 1998). There are a number of methods to establish alcohol quantity and frequency, including direct patient report and drinking diaries and retrospective recording systems (Sobell & Sobell, 2003), although previous reviews have identified that such techniques vary in accuracy (Raistrick, *et al*., 2006). However it should be noted that both of AUDIT scores and typical drinks per day should be adjusted for gender (Dawe, 2002) age

[12] There is a higher risk of developing delirium tremens in those people with a history of seizures or DTs and/or signs of autonomic over-activity with a high blood alcohol concentration.

(both for older adults (Beullens & Aertgeerts, 2004) and adolescents (McArdle, 2008) and established liver disease (Gleeson *et al.,* 2009). Following this initial identification a decision should be made on the setting in which the assisted withdrawal should take place.

The second stage involves an assessment of the presence and severity of alcohol dependence. Again a formal assessment tool is the preferred means to identify the severity of dependence in this guideline.) The review of such tools for this guideline revealed that the Severity of Alcohol Dependence Questionnaire (SADQ, Stockwell *et al.,* 1979; 1983) has broad clinical utility as it identifies the presence and severity of alcohol dependence, predicts withdrawal severity and the quantity of medication to be prescribed during alcohol withdrawal.

Figure 6. Care pathway: withdrawal assessment



5.21.3 Level 3: brief triage assessment

Aims

A brief triage assessment is a filtering process that is undertaken when an individual first contacts a specialist alcohol service, and it has the aim of developing an initial plan of care (MoCAM; DH, 2006). Failure to identify clinical and/or social priorities may result in an individual being directed to inappropriate services or lost to any form of care. Typically people presenting for a triage assessment may be harmful drinkers who have not benefitted from an extended brief intervention see NICE; 2010a) and/or those scoring AUDIT>20), or have been referred to or have self-referred to a specialist alcohol services.

A brief triage assessment is not simply a brief assessment of alcohol problems only. The focus is equally on the management risk, identification of urgent clinical or social problems to be addressed, and accessing pathways of care for alcohol misuse. The triage assessment therefore incorporates the common elements of assessment identified above with the aim of establishing the severity of the individual's problems, the urgency to action required and referral to the most appropriate treatment interventions and provider.

Specifically the triage assessment should establish:

- The need for emergency or acute interventions, for example referral to accident and emergency for an acute medical problem or to a crisis team for a mental health emergency
- Presence and degree of risks of harms to the person, others, and/or children due to alcohol, substance misuse, and comorbid problems (medical, mental health, social and criminal)
- The appropriate alcohol treatment intervention(s) and setting(s) for the problems assessed, for example to an assisted withdrawal for a moderately or severely dependent individual or for a psychological intervention for a harmful or mildly dependent alcohol misusers
- An appropriate level of communication and liaison to all those involved in the direct care and management of the individual
- The need for a further comprehensive specialist assessment (see 1.22.4 below)
- The need for need for and agreed plans for further follow-up

Settings

All specialist alcohol services (including those that provide combined drug and alcohol services) should operate a triage assessment according to agreed local procedures. This level of assessment is not intended to be a full assessment of an individuals' need on which to base a care plan. The Triage Assessment should identify immediate plans of care through the use of standardised procedures to ensure that all clinically significant information and risk factors are captured in one assessment. Incorporating tools and questionnaires as an adjunct to the clinical interview will help improve consistency of decision making.

Methods

The triage assessment should include:

- Alcohol use history including;
    - Typical drinking; setting, brand, and regularity
    - Alcohol consumption using units of alcohol consumed on Typical Drinking Day
    - Features of alcohol dependence (See Level 4 Assessment)

  - Alcohol related problems
  - Adjunctive assessment tools such as the SADQ to inform the assessment of risk and the immediate and future clinical management plan
- Co-ocurring problems (medical, mental health, substance misuse, social and criminal)
- Risk Assessment
- Readiness and motivation to change

Risk Assessment and Evaluation

The increasing importance of risk assessment in the clinical decision making process has lead to a number of tools being developed to systematically screen for high risk problems and behaviours which draw on a common framework for all risk assessment systems in mental health (DH, 2006) . In the NHS it is expected that local protocols are agreed that specify the elements and tools for risk assessment to be applied (MoCAM; DH, 2006). Establishing these protocols and standards will also identify the competencies required for the collation and interpretation of risk to develop a risk management plan.

The risk evaluation process should review all aspects of the information collected during the clinical interview, and where appropriate consider results from; investigations, questionnaire items, correspondence and records, liaison with other professionals, family and carers to formulate an opinion regarding risks to the individual, to others and to the wider community. The evaluation of risk must consider the interaction between comorbid features to arrive at broad opinion of the severity of risk and the urgency to act.

Models of Care for alcohol misusers (MoCAM; DH, 2006) identifies that risk assessment should consider the following domains:

- risks associated with alcohol use or other substance use (such as physical damage, alcohol poisoning)
- risk of self-harm or suicide
- risk of harm to others (including risks of harm to children and other domestic violence, harm to treatment staff and risks of driving while intoxicated)
- risk of harm from others (including being a victim of domestic abuse)
- risk of self-neglect
- safe guarding children procedures must be included

Where risks are identified, risk management plans that consider monitoring arrangements, contingency plans and information sharing procedures need to be developed and implemented (MoCAM; DH, 2006). Guidance developed for those working with patients with mental health problems identified that the best risk assessments and management plans are developed by multi-disciplinary teams and in collaboration between health and social care agencies (DH, 2007).

Urgency to act

The urgency to act will be linked to the severity and level of risks identified from all the information gathered and should consider:

- The individual's intentions to carry out act of self harm or harm to others
- The state of distress being experienced by the individual
- The severity of comorbid medical or mental health conditions and the sudden deterioration of the individual's presentation

- The safeguarding needs of child/young person

5.21.4 Level 4: comprehensive assessment

Aims

A comprehensive assessment should be undertaken where individual needs identify significant comorbid needs, severe alcohol dependence or where a high level of risk factors identified. The characteristics of this group suggest that those referred for comprehensive assessment will often require structured and/or intensive interventions and are often involved with multiple agencies. Those presenting with these complex problems will require their care to be planned and co-ordinated.

The comprehensive assessment aims to:

- determine the exact nature of problems experienced by the individual across multiple domains
- specify needs to form a clear care plan
- identify outcomes to be achieved and methods for measurement

Settings

Comprehensive assessments are undertaken by specialist alcohol services that provide typically tier 3 and 4 interventions although some tier 2 services may also offer comprehensive assessments, as outlined by MoCAM (DH, 2006).

Methods

The comprehensive assessment should not be seen as a single event conducted by one member of the multidisciplinary team, although coordination of the assessment process may bring real benefit (see section 4 for a review of case coordination and care management). The complex nature of the problems faced by an individual with long-standing alcohol misuse or dependence suggests that the full assessment may need to be spread across a number of appointments and typically involve more than one member of the multidisciplinary team. A range of expertise will often be necessary to understand the precise nature of problems that influence the provision and structure of treatment. The comprehensive assessment may require specific professional groups to undertake tasks such as; physical examination, prescribing needs, psychiatric assessment, and a formal assessment of cognitive functioning. Specialist alcohol services conducting comprehensive assessments therefore need to have access, amongst others, to; general practitioners and specialist physicians, addiction psychiatrists, nurses, psychologists and specialist social workers.

The comprehensive assessment should include an in-depth consideration and assessment of the following domains:

- Alcohol Use
    - Consumption
    - Dependence features
    - Problems
- Motivation
- Self-Efficacy
- Problem Domains

  - Substance misuse
  - Physical history and problems
  - Mental health history and problems
  - Social Functioning
- Risk Assessment
- Treatment goals
- Ensuring capacity to consent to treatment
- Formulating a plan of care & evaluating risk

The following sections describe in some detail those aspects of a person health which will require fuller assessment as part of a comprehensive assessment.

5.21.5 Methods of physical investigation

Breath/blood alcohol level

Alcohol is detectable in the breath, and is calibrated reliably with levels of alcohol in the blood. On average it takes approximately one hour to eliminate one unit of alcohol from the body, however the elimination rate of alcohol increases in patients with alcohol dependence (Kater *et al.*, 1969, Ugarte *et al.*, 1977; Allen *et al* 2004). Breath alcometers reliably measure the amount of alcohol currently in the blood in a non-invasive way. A measurement of blood alcohol may be a useful part of the clinical assessment in the following areas:

- In patients with alcohol dependence, taken together with an objective assessment of symptoms of alcohol withdrawal it provides an indication of the severity of physical dependence. Clinicians' judgment about the level of patients' drinking has been found to be inaccurate (Sobell *et al.*, 1979).
- Although self report has been found to be a reliable indicator of levels of alcohol consumption in treatment seeking populations *(*Sobell & Sobell, 2003*),* patients with alcohol in their system at the time of assessment are more likely to underestimate their levels of alcohol consumption *(*Sobell *et al.,* 1990; 1994; Sobell & Sobell 2003).
- Clinicians have a responsibility to discuss drink driving concerns with patients and their responsibilities in reporting this to the DVLA *(DVLA, 2010)*. Patients who have driven to their assessments and who are over the legal limit (80mg/100ml) need to be advised not to drive until they are legally able to do so.

Blood investigations

There are a number of biomarkers that are available which it has been argued may be clinically useful in the assessment of severity of alcohol related physical harm (Allen *et al.*, 2003), monitoring outcome in those individuals, and as a motivational enhancement strategy (Miller *et al.*, 1994). However, in patients who are seeking treatment for alcohol, biomarkers do not offer any advantage over self-report in terms of accuracy of alcohol consumption (Allen *et al.*, 2003; Sobell & Sobell, 2003*),* and are less sensitive and specific than the AUDIT in screening for alcohol misuse (Drummond, 1999).

A raised GGT has a sensitivity of 50-70% in the detection of high levels of alcohol consumption in the last 1-2 months and a specificity of 75-85%. It is the most sensitive and specific of the commonly available laboratory tests, but there are numerous causes for false positive results

including hepatitis, cirrhosis, cholestatic jaundice, metastatic carcinoma, treatment with simvastatin, obesity etc.

Increased mean corpuscular volume (MCV) has a sensitivity of 25%- 52% and specificity of 85-95% in the detection of alcohol misuse. It remains elevated for 1-3 months after abstinence owing to the half-life of red blood cells. Causes of false positives include B12 and folate deficiency, pernicious anaemia, pregnancy and phenytoin (Drummond, 1999; Allen *et al.*, 2004).

The glycoprotein carbohydrate-deficient transferring (CDT) has far greater specificity (80-98%) than other biomarkers for heavy alcohol consumption, and there are few causes of false positive results (severe liver disease, chronic active hepatitis) (Schwan *et al.*, 2004). However routine CDT monitoring is not routinely available, and there remains some debate about how best to measure it. Evidence suggests that the test is less sensitive in women (Anton & Moak, 1994; Anton *et al.*, 2002). CDT increases and recovers more rapidly than GGT in response to a drinking binge, within one week of onset of heavy drinking, and recovery typically in 1-3 weeks, compared with 1-2 months with GGT (Drummond, 1999).

Advantages of blood investigations as part of the initial assessment include:

- screening for alcohol related physical conditions that may need further investigation and onward referral
- Give baseline measures of alcohol related damage (in some patients) against which to measure improvement and act as motivational enhancement strategy
- Objective measurement of outcome, particularly when combined (eg CDT and GGT; Allen *et al.*, 2003) and in conjunction with other structured outcome measures (Drummond *et al.*, 2007).

Hair and sweat analysis

As alcohol is rapidly excreted from the body, there is currently no reliable or accurate way of measuring alcohol consumption in the recent past, and the mainstay of outcome measurement is self-report (Sobell & Sobell, 2003).This is less useful for regulatory monitoring purposes and so there is a growing interest by manufacturers in the design of analytic tests to reliably measure recent alcohol consumption. Studies to date focus on hair and skin sweat analysis, but there is currently a lack of evidence to recommend their use in routine clinical care (Pragst, &. Balikova 2006)

Assessment of alcohol-related physical harm

The assessment of alcohol related physical harm is an important component of a specialist service (Edwards *et al.*, 2003). The aims of such an assessment are to:

- identify physical health problems which require immediate attention and onward referral to appropriate acute medical care
- identify physical health problems which are a consequence of the alcohol misuse, and require monitoring, and potential future referral

The relationship between alcohol related physical health problems and level of alcohol consumption is complex (Morgan & Ritson, 2009). as is the presence of physical signs in relation to underlying pathology. Consequently patients presenting with longstanding, severe alcohol dependency may have few overt physical signs, but significant underlying organ damage (e.g.

liver disease). Others may present with significant symptoms (e.g gastritis) or signs (e.g hypertension) which will resolve without treatment once they reduce the amount of alcohol drunk, or achieve abstinence.

It is important during any clinical assessment to have a high index of suspicion and to identify which conditions require immediate onward referral or monitoring, specifically screening for liver, gastric, cardiovascular and neurological pathology.

Liver/ gastrointestinal problems

Alcohol related liver disease often develops silently over a 10-15year period and blood tests of liver function (Alanine transferase - ALT) may only become abnormal at quite advanced stages of disease and so a test that is within the normal range does not exclude liver damage (Prati et al, 2002)). Other laboratory tests including gamma glutamyl transpeptidase (GGT) and serum aspartate aminotransferase (AST) may be raised in patients with alcohol misuse, but do not necessarily indicate the presence of significant organ damage (Bagrel *et al* 1979)). Patients with signs of severe (decompensated) liver disease (e.g. presenting with jaundice, fluid retention; spontaneous bruising, hepatic encephalopathy will need specialist care from a hepatology service. Symptoms of anorexia, nausea, vomiting and diarrhoea and mal-absorption syndromes are common in patients with alcohol misuse, who are also frequently already prescribed proton pump inhibitors. In the majority of patients, the symptoms resolve with treatment of the underlying alcohol misuse, but patients with significant pain, or evidence of gastro-intestinal blood loss will need referral for further investigation

Cardiovascular

Alcohol has a dose related effect on blood pressure, in addition to being elevated during alcohol withdrawal (Xin *et al.*, 2001). Patients who present with hypertension, or who are already prescribed anti-hypertensive medication will need to have this reviewed as treatment progresses.

Neurological

Wernicke–Korsakoff Syndrome (WKS), classically presents with a triad of symptoms (ataxia, confusion and nystagmus), but in practice this triad only occurs in a minority of cases Thompson and Marshall (2006). Given the severity of disability that may occur if the condition is untreated, clinicians need to have a high index of suspicion particularly in those patients who are ill nourished with any of the following: ataxia, ophthalmoplegia, nystagmus, acute confusional state, or (more rarely) hypotension or hypothermia. Patients presumed to have a diagnosis of Wernicke's encephalophy will need immediate treatment or onward referral (see NICE guideline on management of alcohol-related physical complications, 2010b).

Symptoms of peripheral neuropathy are common (30-70%) in patients with alcohol misuse Monteforte et al The symptoms are predominantly sensory (although muscle weakness is also seen) and include numbness, pain and hyperaesthesia in a 'glove and stocking' distribution primarily in the legs Symptoms should be monitored and will require referral if they do not improve with abstinence.

5.21.6 Mental health: comorbidity and cognitive functioning

Alcohol is strongly associated with a wide range of mental health problems, particularly depression, anxiety, and self harm (Weaver, 2003). In addition, many patients have deficits in

cognitive function which range from the mild to severe, and which may not be identified without systematic investigation (Evert & Oscar-Berman, 1995). The presence of psychological distress and comorbid psychiatric diagnoses, particularly if undetected may have a substantial impact on treatment engagement and progress, leading to sub-optimal treatment outcomes (Weaver, 2003).

There are significant challenges around the assessment and diagnosis of comorbid mental health conditions. Some symptoms may be the direct result of excessive alcohol consumption, or withdrawal, and these tend to reduce once abstinence has been achieved (Brown et al, 1995). The same symptoms may however, also be the result of a co-occurring disorder which requires parallel treatment, but the presence of which may also worsen the alcohol misuse. Finally there are comorbid conditions (e.g. social anxiety, some forms of cognitive impairment) which are not apparent whilst the person is drinking, but which emerge following abstinence and may have an impact on retention in treatment.

Depression and anxiety

Although many symptoms of depression or anxiety are directly attributable to an individual's alcohol misuse, many patients still reach the threshold for a diagnosis of a psychiatric disorder. For instance, 85% of patients in UK alcohol treatment services had one or more comorbid psychiatric disorders including 81% with affective and/or anxiety disorders (34% severe depression; 47% mild depression, 32% anxiety) and 53% had a personality disorder (Weaver *et al.*, 2003). Such high levels of comorbidity are not surprising given that the underlying neurobiology of depression or anxiety and alcoholism have many similarities, particularly during withdrawal (Markou & Koob, 1991). In addition there are shared risk factors since twin studies reveal presence of one increase the risk for the other disorder (Davies *et al.*, 2008).

In community and clinical samples there is a high prevalence of comorbidity between anxiety and alcohol misuse. Anxiety disorders and alcohol dependence demonstrate a reciprocal causal relationship over time, with anxiety disorders leading to alcohol dependence and vice versa (Kushner *et al.*, 1990). Panic disorder and generalised anxiety disorder can emerge from periods of alcohol misuse, however the association with obsessive compulsive disorder is less robust.

Social phobia and agoraphobia frequently predate the onset of alcohol misuse and alcohol consumption. The prevalence of social anxiety ranges from 8-56% which makes it the most prevalent psychiatric comorbidity. Alcohol dependent patients with comorbid social anxiety disorder show significantly more symptoms of alcohol dependence, higher levels of reported depression, and greater problems and deficits in social support networks as compared to alcohol dependent patients without social anxiety (Thevos *et al.*, 1999).

The relationship between alcohol and depression is also bi-directional in that depression can increase consumption, but also can arise from an alcohol misuse (Merikangas *et al.*, 1996).

Sleep disorders

Sleep disorders, commonly insomnia, increase the risk of alcohol misuse and also contribute to relapse (Brower, 2003; Krystal *et al.*, 2008). Whilst many people believe that alcohol helps them sleep, this is not the case. Although onset of sleep may be reduced after drinking alcohol, disruption to sleep patterns occur later in the night such as REM rebound and increased dreaming, as well as sympathetic arousal (Krystal *et al.*, 2008). Abstinence may reveal a sleep

disorder that the person has not been entirely aware of since they have always used alcohol to sleep.

Eating disorders

There is substantial evidence that alcoholism and eating disorders co-occur at high rates (Sinha & O'Malley, 2000). In those presenting for specialist treatment for example, inpatient, rates as high as 40% have been reported. Commonly an eating disorder exists together with other psychiatric disorders such as depression. In those with an eating disorder, up to half have been reported to misuse alcohol (Danksy *et al.*, 2000). A number of studies have found the strongest relationship for bulimia nervosa, followed by patients suffering from binge eating disorder and eating disorder not otherwise specified (EDNOS) (Gadalla *et al.*, 2007). No association has been reported between anorexia nervosa and alcohol misuse. In study of European specialist eating disorder services, alcohol consumption was higher in patients with EDNOS and bulimia nervosa than anorexia nervosa but a greater lifetime prevalence of alcohol use was not found (Krug *et al.*, 2009).

Psychosis

Patients with psychotic disorders (including schizophrenia and bipolar disorder) are vulnerable to the effects of alcohol and at increased risk of using it at levels hazardous to their health (Weaver *et al.,* 2003). Approximately 50% of patients requiring inpatient psychiatric treatment for these disorders will also misuse alcohol (Barnaby, 2003, Sinclair, 2008). However, a smaller proportion of patients will present without a diagnosis made of an underlying psychotic or mood disorder, which will need to be identified as part of a comprehensive assessment. For a more thorough review of this area see the NICE guideline on psychosis and substance misuse (forthcoming NICE, 2011)

Self-harm and suicide

There is a significant, but complex association between alcohol misuse and self harm and suicide. Approximately 50% of all patients presenting to hospital following an episode of self-harm have consumed alcohol immediately before or as part of the act of self-harm (Hawton, 2007). The mortality by suicide in patients who present following an episode of self harm is significantly increased in the next 12 months (66 times that of the general population) (Zahl, 2004) and this risk remains high after many years (Owens, 2002). However recent data from a long term follow up suggests that the mortality of self-harm patients appears to be caused by alcohol related conditions as much as suicide (Sinclair, 2009). For patients whose self-harm occurs only when intoxicated, abstinence from alcohol was recognised as the effective intervention (Sinclair, 2005). Alcohol dependence has been shown to increase the risk of suicide by 5-17 times, with the relative risk being greatest in women (Wilcox, 2004).

Cognitive impairment

Between 75 and 100% of patients admitted for inpatient treatment for alcohol perform below on age standardised tests of alcohol function (Alcohol Strategy Review 2003). Cognitive impairments frequently improve significantly once abstinence has been achieved and so should be reassessed at that time (Loeber *et al.*, 2009).

A number of assessment tools which can be used to assess cognitive function in alcohol misusers have been identified. These include the Mini-Mental Status Examination (MMSE;

Folstein *et al*. 1975); the Cognitive Capacity Screening Examination (CCSE; Jacobs *et al*., 1977); the Neuropsychological Impairment Scale (NIS; O'Donnell and Reynolds, 1983); and the Cognitive Laterality Battery (CLB; Gordon, 1986).

The Mini-Mental Status Examination (MMSE; Folstein *et al*., 1975) is a cognitive screening instrument that is widely used in clinical practice and has been established as a valid and accurate test of cognitive function (Folstein *et al*., 1975). It measures orientation, registration, short term memory, attention and calculation, and language. A score of 17 or less is considered to be severe cognitive impairment, 18 – 24 mild to moderate impairment, and 25 - 30 normal or borderline impairment. It has the advantage of being brief, requiring little training in administration and interpretation, free to use, and is designed to assess specific facets of cognitive function (Small *et al*., 1997). The MMSE has been found to have high sensitivity for detecting moderate to severe cognitive impairment as well as satisfactory reliability and validity (see Nelson *et al*., 1986 for a review). The MMSE can be utilised as a brief screening tool as well as for assessing changes in cognitive function over time (Brayne *et al*., 1997).

It must be noted however that the MMSE has been found to be sensitive to education level in populations where education levels are low (Liu *et al*., 1994; Escobar *et al*., 1986). Therefore, the cut-offs used to identify cognitive impairment may need to be adjusted for alcohol misusers with few years of formal education (Crum *et al*., 1993; Cummings, 1993). Most research evaluating the accuracy, reliability and validity of the MMSE has been in the assessment of age-related cognitive impairment and dementia whereas research in the field of alcohol and substance abuse is limited. However, the MMSE has been utilised in substance abuse research (Smith *et al*., 2006).

The Cognitive Capacity Screening Examination (CCSE; Jacobs *et al*., 1977) was designed to screen for diffuse organic mental syndromes. The CCSE has 30 items which provide information on the areas of orientation, digit span, concentration, serial sevens, repetition, verbal concept formulation, and short term verbal memory. A score of less than 19 has been suggested as indicative of organic dysfunction (Haddad & Coffman, 1987; Hershey & Yang, 1987; Jacobs *et al*., 1977). As with most cognitive screening instruments, the CCSE has been studied extensively in demented populations (Nelson *et al*., 1986). It has been found to have adequate reliability and validity in detecting cognitive impairment (Foreman, 10987; Villardita & Lomeo, 1992). However, the CCSE has been found to be sensitive to age and education (Luxenberg & Feigenbaum, 1986; Omer *et al*., 1983) and has been found to have a high false negative rate and hence low sensitivity (Nelson *et al*., 1986; Schwamm *et al*., 1987). Furthermore, Gillen *et al* (1991) and Anderson *et al.* (1997) reported that the CCSE did not adequately distinguish between cognitively impaired and non-impaired substance abusers.

The NIS is a 50 item scale which has been designed to identify brain damage. The reliability and validity of the NIS has been previously reported in normal and neuropsychiatric populations (O'Donnell *et al*., 1984a; 1984b) as well as having a sensitivity of between 68% and 91% and a specificity of between 43% and 86% (O'Donnell *et al*. 1984b). Errico *et al*., (1990) further reported predictive validity, and test-retest reliability in a sample of alcohol misusers undergoing detoxification.

The CLB was developed to measure visuospatial and verbosequential functioning with tests administered on a sound/sync projector and takes 80 minutes for administration. However, the

CLB has been reported to have limited clinical utility in the assessment of cognitive function in an alcohol dependent population (Errico *et al*., 1991).

Childhood abuse

A history of physical and/ or sexual abuse is high in patients seeking treatment for alcohol misuse, particularly women (Moncrieff and Farmer, 1998). Patients identified with childhood trauma who wish for further intervention should be referred to appropriate services once they have reached a degree of stability in terms of their alcohol use (see NICE, 2005) guideline on PTSD).

Family and relationships

Relationships with partners, parents, children and significant others are often damaged by alcohol misuse (Copello *et al*., 2005). Families and carers also suffer significantly in their own right with an increased incidence of mental disorder (Dawson *et al*., 2007). Involvement of partners or family can help identify the needs of the help seeking individual. The prevalence of alcohol misuse in the victims and perpetrators of domestic violence provides an importance rationale for the exploration of these issues. Similarly sexual abuse has been found to be prevalent in alcohol dependent drinkers seeking treatment and should be assessed with similar sensitivity (Moncrieff & Farmer, 1998; Moncrieff *et al*., 1996).

Employment

The status of the individual's occupation is significant in terms of the individual's ability to remain economically active. Past employment history may indicate the individual's capacity to obtain and retain employment. Employment might provide insights into factors that maintain the individuals drinking status that need to be explored. Those assessing employed individuals will need to consider potential risks to the person, colleagues and the public because of excessive drinking..

Criminality and offending

Criminality and offending behaviour provides an understanding of a number of factors; presence and onset of criminal activity, the severity of offending behaviour, relationship of offending to alcohol consumption and/or alcohol withdrawal and the presence of violence and aggressive behaviour. Liaison with criminal justice services is necessary to ensure appropriate co-ordination of care and effective communication and information sharing protocols are in place.

Fitness to drive

Where an individual with excessive alcohol use identifies that they continue to drive a motor vehicle the healthcare professional must advise the individual that, it is the duty of the license holder or license applicant to notify DVLA of any medical condition, which may affect safe driving. There are circumstances in which the license holder cannot, or will not notify the DVLA. Doctors and health care professionals will need to consult the national medical guidelines of fitness to drive (DVLA, 2010) in these circumstances.

5.21.7 Goals for drinking behaviour

The information collated from the comprehensive assessment will identify the type and severity of the alcohol misuse experienced, and the presence and significance of comorbid problems. This information should be considered alongside the individual's preferred drinking goals, taken at the outset of the assessment, as basis for a negotiated care plan with drinking goals

specified. Previous reviews and studies (Raistrick *et al.*, 2006; Heather *et al.*, 2010; Adamson *et al.*, 2010) have identified that:

- Individuals seeking abstinence from alcohol should be supported in their aim regardless of their severity of problems.

- Individuals with comorbid problems that clearly contra-indicate continued drinking should be strongly advised that abstinence should be considered.

- Individuals who seek non-abstinence goals (i.e. moderation or controlled drinking) usually experience less severe problems and should be supported. However, where a practitioner identifies that abstinence should be promoted but the individual seeks non-abstinence as a goal, a negotiated approach should be supported where abstinence is considered if moderation goals prove unsuccessful.

- If the individual is uncertain as to which goal to pursue, further motivation interventions should be considered to arrive at an agreed approach

- Treatment goals need to be regularly reviewed and changed where indicated. Personnel should adopt a flexible approach to goal setting that recognises the above parameters.

5.21.8 Formulating a plan of care and evaluating risk

The intention of any assessment whether triage, withdrawal or comprehensive is to arrive at a plan of care that takes into account the individual's views and preferences and those of their family and carer's where indicated and any safeguarding issues. The development of a care plan needs to address the presenting alcohol misuse and consider the impact of treatment on existing problems (MOCAM, DH, 2006). It should take account of the presence, severity and complexity of problem areas that in turn will influence the menu of treatment interventions, medications and/or settings that are offered.

Current best practice recommends that a care plan should be developed in negotiation with the individual, (NTA, 2006). The care plan may include short, intermediate and long-term objectives, in addition to any contingency planning needed where risks escalate. Care plans need to be shared with those also involved in providing care to the individual as planned treatment interventions and medications may have significant interactions with existing or planned care for other problems or conditions.

5.21.9 Outcome monitoring

Outcome monitoring is important in assessing how treatment for the alcohol misuse is progressing. The main aim of outcome evaluation should be to assess whether there has been a change in the targeted behaviour due to treatment. Outcome monitoring aids in deciding whether treatment should be continued, or if further evaluation and a change of care pathway is needed. There are three important areas of outcome monitoring; deciding what outcome to measure, how to measure it (the appropriate tools) and when to measure outcome. Routine outcome monitoring (including feedback to staff and patients) has been shown to be effective in improving outcomes (Lambert *et al.*, 2002). It has also been demonstrated that routine session by

session measurement provides a more accurate assessment of overall patient outcomes (Clark *et al*., 2009)

What outcome should be measured?

The general consensus is that assessment of drinking domains (for example, intensity and frequency of drinking) is a basic component of outcome monitoring. For example Emrick (1974) states that monitoring abstinence post-treatment is a significant predictor of psychosocial functioning. Non-drinking domains such as problems or harm have also been suggested to be important in outcome monitoring. Longabaugh (1994) states outcome measurement should contain a range of assessment domains and include life functioning aspects (such as physical health and social needs). Secondary analyses of Project MATCH concluded that alcohol problems was the only nondrinking domain which was significantly associated with drinking outcome measures (percent days abstinent, drinks per drinking day, first drink) (Project MATCH Research Group, 1997; 1998). This indicates that other domains may need to be assessed separately to drinking related outcome measures, perhaps the use of the APQ on a regular but infrequent basis (for example, at 3 to 6 months intervals) may be one way to capture these problems

How should outcome be measured?

The methods of outcome monitoring should be appropriate for a clinical patient population. The outcome measure that is applicable to all tiers of services is assessing the level of alcohol consumption by asking the patient about their intensity and frequency of drinking but the use of a formal measure may increase the likelihood that this will be done in a reliable manner. The AUDIT questionnaire is already widely used and draws on the intensity and frequency of alcohol consumption (in particular the first three questions from the questionnaire). The time taken to complete the AUDIT (less than 2 minutes) also lends itself to use in routine services. The AUDIT-C (Bush *et al*., 1998) is a three-item sub-scale of the AUDIT which evaluates alcohol consumption; i.e. frequency of drinking, quantity consumed on a typical occasion and the frequency of heavy episodic drinking (six or more standard drinks on a single occasion). Bush *et al* (1998) reported that the AUDIT-C performed better than the full AUDIT in detecting heavy drinking and was just as effective as the full AUDIT in identifying active alcohol abuse or dependence. The study also found that using a cut-off of 3 out of a possible 12 points, the AUDIT C correctly identified 90% of active alcohol abuse/dependence, and 98% of patients heavy drinking. However, other studies have reported that a cut-off of 5 or more for men and 4 or more for women results in the optimal sensitivity and specificity for detecting any alcohol use disorders (Gual *et al*., 2002; Dawson *et al*., 2005). In addition, the AUDIT-C has been found to be equally as effective in detecting alcohol use disorders across ethnic groups (Frank *et al*., 2008). However, it should be noted that the AUDIT-C has been reported to have a high false positive rate when used as a screening tool (Nordqvist *et al*., 2004). However, the ease of use, and already established relationship between frequency and quantity of drinking with alcohol abuse and dependence give the AUDIT-C credence for the use of outcome monitoring. An alternative is a weekly drinking diary referring to the last week.

When should outcome be measured?

Previous research indicates that most changes in drinking behaviour and the largest reduction in severity of drinking occurs in the first three months of treatment and benefits are maintained up to 12 months (Babor *et al*., 2003; Weisner *et al*., 2003). Initial benefits in drinking related outcomes maybe more apparent at three months but other nondrinking domains such as social

functioning and global health may need longer to show global benefits of treatment. It is also the case that there is a high attrition rate in many alcohol services and so the risk of poor response rates to routine outcome measurement is correspondingly high. This argues for routine session by session completion and would again favour the use of a brief measure such as the AUDIT or the feedback from a weekly drinking diary. The AUDIT as the advantage that it can be quickly completed at the beginning of treatment session, constructing a drinking diary in such a situation would be both time consuming and less reliable.

5.21.10 Evidence summary

Assessment tools

A summary of the evidence for the assessment tools is presented in Section 1.20 above.

In addition to these assessment domains, the GDG also considered what measures might usefully be used for routine outcome monitoring. Alcohol consumption (frequency and intensity) was identified as the most important outcome and although self report can be an effective measure when used in the correct context, more formal ratings, for example, such as alcohol diaries may have greater reliability. The AUDIT which asses both frequency and intensity of drinking is in widespread use and is quick to complete. The GDG therefore favoured the AUDIT (specifically the first three questions from the questionnaire will subsequent questions only used for 6 month follow up) as a routine measure but recognised that in some services, especially Tier 3 and 4 specialist services additional more detailed, assessment measure may also be routine used.

Content of the clinical assessment

Although the review began with a consideration of the validity of a range of assessment tools, it was intended that these measures should be an adjunct to a structured clinical interview. Review of the literature identified a number of components of a structured clinical interview. These included assessment of the current extent and history of drinking, associated potential for withdrawal, the likelihood of withdrawal, the need for review of associated physical health problems, the examination of mental health and the impact of alcohol on social, personal and occupational and educational functioning. It also identified that the impact of alcohol on the family would be an important issue also to be considered. Considerable emphasis on the literature reviewed was placed on the importance of engaging people with alcohol related problems in treatment and negotiating appropriate goals. It is clear from the literature that for people who are moderate and severe drinkers, the initial goal should be one of abstinence. For others who are harmful and mildly dependent drinkers, it may be possible to consider a reduction in drinking as a reasonable treatment goal. However, past history of unsuccessful attempts to moderate drinking should be born in mind when making these assessments.

The review of formal assessment measures also considered a number of measures of motivation (readiness for change). It was not felt by the group that the quality of these measures (in part because of impracticality of these measures which were designed primarily for use in research) warranted their use in standard clinical care. However, a consideration of a patient's readiness and/or motivation for change is a vital part of assessment.

Physical investigations

This chapter also covered the role of physical investigations in the treatment, assessment and management of people with alcohol misuse. It has already been acknowledged that an awareness of, and inquiry into the nature of commonly presenting physical health problems with alcohol misuse are important. This guideline, and other related NICE guidelines (NICE 2010a, 2010b), considered the value of biomarkers, for example, liver function tests as indicators for diagnosis of alcohol misuse. From the reviews conducted for this and the other NICE guidelines it was concluded that these measures have insufficient sensitivity and specificity compared to validated assessment methods such as the AUDIT. However, for people with specific physical health problems, for those whom regular feedback on a particular measure may act as a motivational tool and those for whom pharmacological treatments may require biological tests, for example, naltrexone and disulfiram, then these measures may have an important part to play in the ongoing treatment and management of alcohol related misuse. No evidence was identified in this or the other NICE guidelines (2010a; 2010b) to support the use of other biomarkers for example, hair analysis, for routine clinical use in assessment or outcome monitoring of alcohol misuse.

Assessment of comorbid substance misuse

It is recognised that smoking, drinking and drug taking behaviours cluster together (Farrell *et al.*, 2001) and that excessive drinkers with high AUDIT scores are more likely to have used drugs in the past (Coulthard *et al.*, 2002). Therefore the evidence suggests that co-existing substance misuse should be explored in relation to excessive alcohol consumption to identify potential risk and the occurrence of adverse interactions between substances and/or comorbid medical or mental health problems. Guidance on substance misuse (NICE 2008) recommends that questions on drug misuse should be consider as part of a routine clinical assessment including the type of drug and its administration, the quantity and the frequency with which it is used.

Assessment of comorbid mental health problems

Mental health problems which co-exist with alcohol misuse can have a significant impact, both on the treatment and long-term outcome of the alcohol related problem. However, depression and anxiety can often develop as a consequence of alcohol misuse. At assessment there is no reliable way of determining comorbid mental health problem is caused by or consequent on the alcohol misuse. This means that symptoms of comorbid mental disorder need to be monitored throughout the course of assessment and treatment. (psychotic disorders are relatively uncommon in alcohol misusers: for advice on the treatment and management of alcohol and psychotic disorders see NICE guideline 2011a). A common presentation in alcohol misuse is suicidal ideation. This needs to be assessed and actively managed as part of an overall risk management process. Where necessary the evidence suggests that a suicide prevention plan and action should be considered where there is a serious risk of suicide. The GDG considered that as, a minimum, the assessment of common mental disorders should occur three to four weeks following abstinence from alcohol. At this point, consideration may be given to treatment of the specific mental disorder if it persists or referral to appropriate mental health services. There is no evidence that a pre-existing but successfully treated alcohol misuse would impact on the treatment of a mental disorder and the relevant NICE guideline should be consulted.

Cognitive impairment

Mild cognitive impairment is present when many patients present with alcohol misuse. These mild impairments, which may be transitory, are, however, often missed in the initial

assessment. The evidence reviewed suggested that the MMSE has reasonable validity as an initial identification tool, perhaps supplemented with specific questions to detect duration extent or functional impairment of the mental disorder. It is not possible, particularly with people who are actively abusing alcohol to conduct an effective cognitive assessment. Unless there is evidence of gross cognitive impairment, which may require further and immediate investigation, the GDG took the view that adequate assessment of cognitive impairment is best left until 3-4 weeks following abstinence from alcohol. At this point if significant cognitive impairment persists it should be subject to more formal assessment including a detailed history and neuropsychological testing. Those patients presenting acutely with a confused state and significant memory loss, may be suffering from Wernicke's encephalopathy and should be assessed and treated accordingly (see NICE guideline 2010b).

Organisation and delivery of assessment

The evidence reviewed for the organisation and delivery of the range of assessment covered in this guideline are reviewed in a number of places in this guideline, including the review of the organisation of stepped care and case management systems in section 3 of this chapter on the organisation and delivery of services and readers are referred to that chapter for a full summary). In addition, the current provision of existing assessment treatment systems and, in particular, the MOCAM framework was reviewed. This approach begins with an initial case identification/diagnostic assessment. Here the emphasis is on brief assessments which can be administered by staff from a range of services in health care and related settings. There is good evidence from the assessment tools reviewed above that scores on measures such as the AUDIT and SADQ provide reasonably good indicators, in the context of overall clinical assessment, of the appropriate level of intervention. There is also evidence that service users presenting with harmful drinking and/or dependence can be assessed in a relatively brief triage assessment. The guideline also reviewed the evidence for those factors to be considered in a withdrawal assessment (draw on the evidence for appropriate settings for administration of inpatient or community base withdrawal In summary the GDG felt that, in the absence of any evidence to the contrary, a stepped approach to assessment in line with that set out in the MoCAM (DH, 2006) document was the right approach to take.

Outcome monitoring

The GDG reviewed the evidence for the use of routine outcome monitoring. A variety of assessment tools were considered as part of the overall view of assessment tools. Although these measures are effective at identifying the presence or severity of the disorder none were felt suitable for routine outcome measurement. The evidence suggested that relatively simple but structured measures of alcohol consumption measuring such as the frequency and intensity of drinking and the AUDIT (in particular the first three questions from the questionnaire, the AUDIT-C) were the preferred routine outcome measures with the later perhaps offering a more reliable and efficient means of monitoring. There is also evidence that self assessment, if used in an appropriate and supportive relationship was as good an indicator as any of the routine outcome measurements. The use of breath test for alcohol was felt not to be an appropriate measure given its relatively short period of time that alcohol is present in the body, although it may have a use in patient monitoring withdrawal programmes, or to assess whether someone has been drinking during a therapeutic intervention.

5.22 From evidence to recommendations

Assessment tools

The review of assessment tools identified a number of measures which had sufficient psychometric properties to be used in routine clinical care. In addition to these factors, the feasibility of their use in routine care also influenced the Guidelines Development Group's decisions. As an initial case identification tool and as one which would indicate whether or not further treatment was required, the AUDIT questionnaire is the most appropriate instrument. On occasions where the AUDIT questionnaire was not available and/or not practical, then a simple daily alcohol consumption measure could also be used as an indicator of potential need for treatment. For people who were suspected of having alcohol dependence, the use of the Severity of Alcohol Dependence Questionnaire (SADQ) or the Leeds Dependence Questionnaire (LDQ), were supported by the GDG as they were deemed effective instruments to measure the severity of alcohol dependence in order to guide further management. For assessing the extent of problems associated with alcohol misuse the Alcohol Problems Questionnaire (APQ) was identified as meeting all the criteria. In addition, on the basis of the NICE guideline on the management of alcohol-related physical complications review (NICE 2010b), for the measurement of withdrawal symptoms the CIWA-Ar was judged to be the most appropriate instrument.

Content of the clinical assessment and the organisation and delivery of assessment systems

It is important to recognise that the use of individual assessment tools alone, such as those identified above, does not constitute a comprehensive assessment. The evidence suggested that, in addition to a past and current history of drinking, the associated physical and mental health problems and the impact on health and social and economic problems should also be considered. This section also identified the importance of the impact on family (including importantly children). It is also important to recognise that a key aspect of effective assessment is the process of engaging people and identifying treatment goals. For example, determining whether abstinence, which is the initial preferred goal for moderate and severe drinkers or a reduction in alcohol consumption, is the preferred goal. The GDG therefore decided to provide detail on the content of the range of assessments. The GDG also carefully reviewed the evidence for t the organisation and delivery of assessment systems and saw no reason to veer from the established system recommended within MoCAM (DH, 2006). This may require additional specialist assessment resources and systems to ensure that individuals have the capacity and competency deliver these assessments.

Physical investigations

The review for this guideline (based in significant part on parallel work undertaken on other NICE guidelines , NICE ; 2010b) established that physical investigations in particular, blood tests including measures of liver function are not sufficiently sensitive or specific measures for routine use in specialist alcohol services. However, biomarkers can be useful as motivational tools by providing feedback on progress and in assessing suitability for some pharmacological interventions (for example, naltrexone and disulfiram). The GDG also considered that the measurement of breath alcohol is a useful, objective part of the clinical assessment in withdrawal and that biomarkers may be helpful to identify the client's level of tolerance to alcohol.

Assessment of comorbid substance misuse

The presence of comorbid substance misuse is associated with poorer outcomes for those with alcohol misuse the GDG reviewed evidence on this along with the recommendation in the NICE

(2008) guideline on psychosocial management of substance misuse. It was agreed that assessment of comorbid drug misuse should therefore be a part of routine assessment of alcohol misuse. Consideration should be given to the use of use biological testing (for example, of urine or saliva samples) as part of a comprehensive assessment of drug use, but they should not rely on it as the sole method of diagnosis and assessment.

Assessment of comorbid mental health problems

Comorbid mental health problems are a common presentation in alcohol misusers. It is important that this is assessed at initial presentation. However, it should be noted that for most clients symptoms of for example, depression and anxiety will remit following abstinence from alcohol. It is therefore often not appropriate or necessary to instigate a treatment for the disorder at the point of the initial assessment. However, careful monitoring and reassessment of mental health symptoms following abstinence are an important part of the assessment procedure. Treatment of mental health disorders persisting beyond 3-4 weeks after abstinence should be considered.

Routine outcome monitoring

Routine outcome monitoring is an essential part of any effective health care system provision. The use of formal measures was not supported by the review. Alcohol consumption (including intensity and frequency) was identified as the most reliable measure and there is good evidence that self report if used within the context of a supportive non-judgmental relationship is an effective outcome measure. Simple systems for formalising self-report should therefore form the routine outcome measurement system (such as the AUDIT-C questionnaire).

Competence of staff

Throughout this guideline the assumption is that individuals are competent to deliver them. There is good evidence to suggest that without effective training, skills and competence, assessment systems are likely to fall short of their requirements. It is therefore essential that individuals performing these assessments should be fully competent to do so.

5.22.1 Recommendations

Identification and assessment in all settings

5.22.1.1 Make sure that assessment of risk is part of any assessment, that it informs the development of the overall care plan, and that it covers risk to self (including unplanned withdrawal, suicidality and neglect) and risk to others.

5.22.1.2 Staff working in services provided and funded by the NHS should be competent to identify harmful drinking and alcohol dependence. They should be competent to initially assess the need for an intervention or, if they are not competent, to refer the service user to a service that can provide an assessment of need. [KPI]

5.22.1.3 When conducting an initial assessment, as well as assessing alcohol misuse, the severity of dependence and risk, consider the:

- extent of any associated health and social problems

- need for assisted withdrawal.

5.22.1.4 Use formal assessment tools to assess the nature and the severity of alcohol misuse, including the:

- AUDIT[13] for identification and as a routine outcome measure
- SADQ[14] or LDQ[15] for severity of dependence
- CIWA-Ar[16] for severity of withdrawal
- APQ[17] for the nature and extent of the problems arising from alcohol misuse.

5.22.1.5 When assessing the severity of alcohol dependence and determining the need for assisted withdrawal, adjust the criteria for women, older people, children and young people[18], and people with established liver disease who may have problems with the metabolism of alcohol.

5.22.1.6 Staff responsible for assessing and managing assisted alcohol withdrawal (see 5.30.2) should be competent in the diagnosis and assessment of alcohol dependence and withdrawal symptoms and the use of drug regimens appropriate to the settings (for example, inpatient or community) in which the withdrawal is managed.

5.22.1.7 Staff treating people who are alcohol dependent presenting with an acute unplanned alcohol withdrawal should refer to 'Alcohol use disorders: diagnosis and clinical management of alcohol-related physical complications' (NICE clinical guideline 100).

Assessment in all specialist alcohol settings

Treatment goals

5.22.1.8 In the initial assessment in specialist alcohol settings of all people who misuse alcohol, agree the goal of treatment with the service user. For harmful drinking and mild dependence the aim should be abstinence or a moderate level of drinking that is pre-

13 Alcohol Use Disorders Identification Test: Babor, T.F., Higgins-Biddle, J.C., Saunders, J.B., et al. (2001) *AUDIT: The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care* (2nd ed). Geneva: World Health Organization.

14 Severity of Alcohol Dependence Questionnaire: Stockwell, T., Hodgson, R., Edwards, G., et al. (1979) The development of a questionnaire to measure severity of alcohol dependence. *British Journal of Addiction to Alcohol and Other Drugs*, 74, 79-87. Stockwell, T., Murphy, D., Hodgson, R. (1983) The severity of alcohol dependence questionnaire: its use, reliability and validity. *British Journal of Addiction, 78*, 145-155.

15 Leeds Dependence Questionnaire: Raistrick, D., Bradshaw, J., Tober, G., et al. (1994) Development of the Leeds Dependence Questionnaire (LDQ): a questionnaire to measure alcohol and opiate dependence in the context of a treatment evaluation package. *Addiction, 89*, 563-572.

16 Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised: Sullivan, J.T., Sykora, K., Schneiderman, J., et al. (1989) Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *British Journal of Addiction*, 84, 1353-1357.

17 Alcohol Problems Questionnaire: Drummond, C. (1990) The relationship between alcohol dependence and alcohol-related problems in a clinical population. *British Journal of Addiction, 85*, 357-366.

18 See section 1.3.9 for assessment of children and young people.

determined and agreed by both staff and the service user. For moderate and severe dependence or significant medical or psychiatric comorbidity the aim should be abstinence in the first instance.

5.22.1.9 When developing treatment goals, consider that some people who misuse alcohol may be required to abstain from alcohol as part of a court order or sentence.

Brief triage assessment

5.22.1.10 All adults who misuse alcohol who are referred to specialist alcohol services should have a brief triage assessment to assess:

- the history and severity of the alcohol misuse (using AUDIT) and severity of dependence (using SADQ)
- the need for urgent treatment including assisted withdrawal
- any associated risks to self or others
- the presence of any comorbidities or other factors that may need further specialist assessment or intervention.

Agree the initial treatment plan, taking into account the service user's preferences and outcomes of any previous treatment.

Comprehensive assessment

5.22.1.11 Consider a comprehensive assessment for all adults referred to specialist services who score more than 15 on the AUDIT. A comprehensive assessment should assess multiple areas of need, be structured in a clinical interview, use relevant and validated clinical tools (see 5.22.1.4), and cover the following areas:

- alcohol use, including:
    - consumption: historical and recent patterns of drinking (using, for example, a retrospective drinking diary), and if possible, additional information (for example, from a family member or carer)
    - dependence (using, for example, SADQ or LDQ)
    - alcohol-related problems (using, for example, APQ)
- other drug misuse
- physical health problems
- psychological and social problems
- cognitive function (using, for example, MMSE)[19]

[19] Mini-Mental State Examination: Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975) 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychological Research*, 12, 189–198.

- readiness and belief in ability to change. **[KPI]**

5.22.1.12 Assess comorbid mental health problems as part of any comprehensive assessment, and throughout care for the alcohol misuse because many comorbid problems (though not all) will improve with treatment for alcohol misuse. Use the assessment of comorbid mental health problems to inform the development of the overall care plan.

5.22.1.13 For service users whose comorbid problems do not significantly improve after abstinence from alcohol (typically after 3–4 weeks), consider providing or referring for specific treatment (see the relevant NICE guideline for the particular disorder).

5.22.1.14 Consider measuring breath alcohol as part of the assessment for and management of assisted withdrawal. However, breath alcohol should not typically be measured for routine monitoring in alcohol treatment programmes.

5.22.1.15 Consider blood tests to help identify physical health needs, but do not use blood tests routinely for the identification and diagnosis of alcohol misuse.

5.22.1.16 Consider brief measures of cognitive functioning to help with treatment planning (for example, MMSE). Formal measures of cognitive functioning should typically only be performed if the impairment persists after a period of abstinence or a significant reduction in alcohol intake.

Section 4 – Determining the appropriate setting for the delivery of effective care

5.23 Introduction

This section is concerned with identifying the setting(s) in which to deliver clinical and cost-effective care for people who misuse alcohol. It begins with a review of planned assisted withdrawal, which is linked to and draws heavily on the review conducted for the NICE guideline on management of alcohol-related physical complications (NICE, 2010b). It then considers the range of settings in which assisted withdrawal and the interventions covered in Chapters 6 and 7 of this guideline may be best provided, including community, residential and inpatient settings.

The majority of services provide treatment for alcohol misuse in community or outpatient settings, whereby a patient is visited at home by a health or social care professional or attends a clinic or a day hospital. There are also approximately 200 voluntary or independent sector providers of residential rehabilitation treatment for drug or alcohol problems in England (National Treatment Agency for Substance Misuse, 2009). The services that they offer can be differentiated according to factors such as the principal aims of treatment, patient group and length of stay. Residential rehabilitation services may offer medically assisted withdrawal from alcohol, but usually only as a prelude to longer-term rehabilitation or aftercare. Finally, medically-managed inpatient facilities are usually run by the NHS, and a review of national provision in 2004 highlighted 77 NHS hospitals that admitted patients for drug or alcohol withdrawal, and a further 28 non-statutory or private providers (Day, 2005).

Current practice in the management of assisted withdrawal, and the general provision of alcohol treatment services, tends to follow MoCAM (DH, 2006) guidance which suggested that community settings were preferred for the treatment of the majority of alcohol misusers, as they are sees as more cost effective and more likely to promote change in their drinking behaviour in a normal social environment. However, it was noted that some people would require treatment in hospital or in supported residential accommodation, including those who are severely dependent, have a history of withdrawal complicated by seizures or delirium tremens (DTs), are in poor physical or psychological health, are at risk of suicide, or misuse drugs. Homeless people, those who lack social support or stability or those who have had previous unsuccessful attempts at withdrawal in the community may also require inpatient treatment. MoCAM also stipulated that inpatient assisted withdrawal should lead seamlessly into structured care-planned treatment and support, whether delivered in the community or in residential rehabilitation services. However, it should also be noted, as discussed at the beginning of this chapter, that there is considerable variation in practice including in the settings in which services are provided

A number of authors have considered the possible benefits of treatment in a residential setting (Gossop, 2003; Mattick & Hall, 1996; McKay *et al*., 1995; Weiss, 1999). In considering the potential benefits of any setting it is useful to distinguish between the provision of withdrawal management and the provision of further treatment and rehabilitation. Residential settings provide a high level of medical supervision and safety for individuals who require intensive physical and/or psychiatric monitoring, and the possibility of more intensive treatment may

also help patients who do not respond to interventions of lower intensity. Residential settings may also offer the patient respite from their usual social milieu (that is, the people and places associated with alcohol use) and improved continuity of care. However, the protectiveness of a residential unit may also be one of its main disadvantages—it may limit opportunities for the patient to develop new coping strategies (Annis, 1996). Time away from work or study, reduced family contact and the stigmatisation associated with some residential service settings may also be potential disadvantages of residential care (Strang, 1997). Finally, residential settings are considerably more expensive than non-residential alternatives.

Previous reviews of studies of residential treatment for alcohol misuse conducted in the 1980s concluded that residential/inpatient treatment had no advantages over outpatient treatment (Annis, 1996; Miller, 1986). Furthermore, every controlled study of length of inpatient treatment found no advantage in longer over shorter stays, or in extended inpatient care over assisted withdrawal alone (Annis, 1996; Miller, 1986). However, the authors noted a variety of methodological problems with the studies, not least that the nature of the treated populations varied substantially, from general psychiatric patients assessed for alcohol misuse and outpatient problem drinkers to inpatient alcoholics (Miller, 1986). Miller (1986) also noted that a course of outpatient treatment averaged less than 10% of the cost of inpatient treatment. Therefore, even if residential settings afforded a modest advantage in overall effectiveness, preference might still be given to non-residential treatment based on cost effectiveness.

Further research conducted since the mid-1980s has challenged some of these conclusions. In a review of the literature, Finney and colleagues (1996) found 14 studies in which setting effects might have been detected. Of these studies, seven found significant setting effects on one or more drinking-related outcomes, with five favouring inpatient over outpatient treatment and a further two favouring day hospital over inpatient treatment (Finney *et al.*, 1996). In all but one instance in which a significant effect emerged, patients in the more effective setting received more intensive treatment, and participants were not 'pre-selected' for their willingness to accept random assignment. Other potential methodological problems were also identified. As mentioned above, it is often thought that an inpatient or residential setting will benefit patients from social environments where heavy drinking is common and encouraged by allowing the patient a period of respite. However, some studies randomised participants to inpatient or outpatient treatment after an initial period of inpatient treatment for medically-assisted withdrawal. Finney and colleagues (1996) commented that this treatment setting contamination might bias studies toward no-difference findings.

5.24 Clinical questions

1. In adults in planned alcohol withdrawal, what is the clinical efficacy, cost effectiveness, safety of, and patient satisfaction associated with:
   - preparatory work before withdrawal
   - different drug regimens
   - the setting (that is, community , residential or inpatient)?

2. In adults in planned alcohol withdrawal what factors influence the choice of setting in terms of clinical and cost effectiveness including:
   - severity of the alcohol disorder

- physical comorbidities
- psychological comorbidities
- social factors?

3. In adults with harmful or dependent alcohol use what are the preferred structures for and components of community-based and residential specialist alcohol services to promote long-term clinical and cost-effective outcomes?

5.25 Assisted withdrawal

5.25.1 Introduction

This section is essentially concerned with planned assisted withdrawal. It should be read in conjunction with the NICE guideline on management of alcohol-related physical complications (NICE, 2010b); the reviews conducted for that guideline informed the decisions of the GDG. Previous research assessing the settings for assisted withdrawal from alcohol has yielded a considerable amount of debate about the safety, efficacy and cost effectiveness of the various options available. Settings for assisted withdrawal include the community, where assisted withdrawal may be delivered in a day hospital setting, in specialist community alcohol teams or in primary care, and specialist inpatient and specialist residential settings. In addition, assisted withdrawal programmes are also provided in the prison healthcare system and in a range of acute general medical settings. This section is also concerned with the patient indications for inpatient assisted withdrawal. Some further details about the settings in which assisted withdrawal can take place are given below.

Community settings

In a community setting a person undergoing assisted withdrawal lives in their own accommodation throughout the treatment. A spectrum of treatment intensity is also possible. Day hospital treatment (sometimes known as 'partial hospitalisation') may involve the patient attending a treatment facility for up to 40 hours per week during working hours, Monday to Friday, and returning home in the evening and weekends. This facility may be located within an inpatient or residential rehabilitation unit, or may be stand-alone. It is likely to be staffed by a multidisciplinary team, with input from medical and nursing staff, psychologists, occupational therapists, social workers, counsellors, and other staff specialising in debt, employment or housing issues. Other community assisted withdrawals may invite the patient to attend for appointments with a similar range of multidisciplinary staff, but at a much lower frequency and intensity (for example, once or twice a week), or they may be provided by GPs often with a special interest in treating alcohol-related problems. Alternatively, staff may visit the patient in their own home to deliver interventions. Between these two options are most intensive community-based options, where an increased frequency of community visits and some limited use of office or team-based treatment may form part of an intensive community programme.

Inpatient and residential settings

In inpatient and residential settings, the service user is on-site for 24 hours a day for the duration of assisted withdrawal. Inpatient and residential settings encompass a spectrum of treatment intensity. At one end lie specialist units within either acute medical or psychiatric

hospitals, dedicated to the treatment of alcohol or drug problems (known as 'inpatient units'). Such units have specialist medical and nursing input available 24 hours a day, and are staffed by a multidisciplinary team that may also include psychologists, occupational therapists, social workers, counsellors, and other staff specialising in debt, employment or housing issues. At the other end are facilities usually known as 'residential rehabilitation' units, which are usually run by the non-statutory sector and not sited within hospital premises. Although the goal of such units is usually the provision of longer-term treatment (3 to 12 months) aimed at enhancing the patient's ability to live without using alcohol, increasingly they also provide an initial period of assisted withdrawal. Such units may also have access to medical and nursing input over the full 24-hour period, but this is usually at a lower level of intensity and more likely to utilise non-specialist staff (for example, GPs). Such units are more likely to adopt a 'social model' rather than a 'medical model', and may be staffed by both professionals and individuals in recovery. In addition, a number of prisons may offer a high level of medical supervision including, where necessary, admission to the hospital wing of the prison.

5.25.2 Aim of review and review protocol

The initial aim of this review was to perform a systematic meta-analysis of RCT data that addressed the clinical question. However, only one well-designed RCT assessing the benefits and harms of different settings for assisted withdrawal has been published (Hayashida *et al*., 1989). Therefore, the GDG made a consensus-based decision to assess all available studies and provide a narrative review. The review team assessed the literature identified from the search conducted by the NICE guideline on management of alcohol-related physical complications (NICE, 2010b); full details of the search strategies can be found in that guideline. Studies were considered for inclusion in a narrative review for this guideline if they met the inclusion criteria (see Chapter 3) and if the population being assessed in the study reflected the scope of this guideline (see Appendix 1). Furthermore, studies were considered for inclusion in the narrative review using the clinical review protocol in Table 1. The key outcomes of interest were: the efficacy of the setting for assisted withdrawal (for example, the patient successfully completed the programme and remained abstinent during the period assisted withdrawal); the safety profile (for example, the development of complications, and hence the patient factors that indicate that a non-residential setting for assisted withdrawal is unsuitable and unsafe); and participation in consequent rehabilitation treatment. Other outcomes of interest are patient satisfaction and other patient and physician related factors.

Table 19: Clinical review protocol for the evaluation of different settings for assisted withdrawal from alcohol

Electronic Databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO; see the NICE guideline on management of alcohol-related physical complications (NICE, 2010b) for search strategies
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs; Systematic reviews
Patient population	Adults (>18 years) Patients with alcohol withdrawal syndrome
Critical Outcomes	Main outcomes: severity of withdrawal; completion rates; abstinence during assisted withdrawal; safety (development of complications); participation in further rehabilitation treatment after assisted withdrawal Other outcomes; patient and physician factors

5.25.3 Studies considered

Five studies comparing different settings for assisted withdrawal were identified. Of these, one was an RCT (Hayashida *et al*., 1989), three were retrospective matching studies (Stockwell *et al*., 1991; Bartu & Saunders, 1994; Parrott *et al*., 2006), and one a retrospective case study comparing patient characteristics in different settings (Allan *et al*., 2000). In addition, five open prospective studies (Collins *et al*., 1990; Drummond & Chalmers, 1986; Feldman *et al*., 1975, Soyka & Horak, 2004; Stinnett, 1982) and an RCT assessing adding a brief psychological intervention to home-based assisted withdrawal (Alwyn *et al*., 2004) were also identified.

5.25.4 Narrative review of settings for assisted withdrawal

Only one randomised trial (Hayashida *et al*., 1989), conducted in a US Veterans Administration medical centre, compared the effectiveness, safety and cost of inpatient (n=77) and outpatient (n=87) assisted withdrawal. Patients with serious medical or psychiatric symptoms, predicted delirium tremens and a very recent history of seizures were excluded from this study. The authors reported that more inpatients than outpatients completed assisted withdrawal. However, inpatient treatment was significantly longer and more costly than outpatient treatment. Additionally, both groups had similar reductions in problems post-treatment when assessed at 1- and 6-month follow-up. Although abstinence was statistically significantly higher for the inpatient group at 1-month follow-up, these differences were not observed at 6-month follow-up. The authors concluded that outpatient assisted withdrawal should be considered for people with mild-to-moderate symptoms of alcohol withdrawal.

Stockwell and colleagues (1991) compared a retrospective inpatient sample (n=35) with a group receiving home-based assisted withdrawal (n=41). The two samples were matched for age, sex, and drinking severity. Patients undertaking home-based assisted withdrawal were severely dependent (SADQ score = 28.7; average 174.6 units per week) and had a high level of alcohol-related problems (APQ score = 4.6). The authors reported that home-based assisted withdrawal was as safe and effective for a severely dependent population as inpatient care. However, the matched inpatient sample did not include anyone with severe alcohol withdrawal syndrome or physical or psychiatric symptoms and, therefore, is not representative of an inpatient population.

Bartu and Saunders (1994) also compared people undertaking home-based assisted withdrawal (n=20) with patients in an inpatient specialist unit (n=20). Patients were matched for age, sex, presence of a supporter, absence of medical complications, and severity of withdrawal symptoms. It was reported that home-based assisted withdrawal was as beneficial as inpatient assisted withdrawal. It should be noted, however, that the matched inpatient sample was not representative of a typical inpatient, who may be severely dependent and have several complications.

Parrott and colleagues (2006) compared alcohol-focused outcomes and cost of residential (n=54) and any day (n=49) settings for assisted withdrawal in the UK and reported similar alcohol-focused outcomes (percent days abstinent and drinks per drinking day) for patients attending a residential treatment centre and a day treatment centre in the UK. This paper mainly discusses cost implications and is reviewed in the health economics section (1.3.5).

In a comparison between home-based assisted withdrawal (n=29) and day hospital services (n=36), in severely dependent patients, Allan and colleagues (2000) in a UK-based study evaluated the types of patients selected for home-based assisted withdrawal, its safety and efficacy, and patient satisfaction and involvement in further treatment. Participants in both groups were severely dependent (two thirds had SADQ score > 30), although the day hospital group drank significantly more at baseline (home-based group = 178 units, day hospital group = 194 units in the week before assisted withdrawal). Furthermore, although both groups had alcohol-related problems, as assessed by the APQ, the day hospital group had significantly more severe problems and social instability. The authors reported that there were no significant differences between the groups in the proportion of participants who completed assisted withdrawal, complication rates (which were low), and uptake of treatment post withdrawal. However, it should be noted that this study did not match participants in both settings but aimed to assess the characteristics of the patients who use home-based and day hospital assisted withdrawal.

Apart from the Hayashida and colleagues (1989) study, the studies discussed above were observational in design and participants were only matched for severity of alcohol dependence. Furthermore, although these studies indicated that it is feasible for assisted withdrawal to take place in a community setting for a severely dependent population, it is probable that a number of patients with significant comorbidities and previous history of seizures where excluded. As these patients form a significant proportion of those who are referred to and receive inpatient or residential assisted withdrawal, caution is needed when considering these results.

Further studies assessing the treatment outcomes and characteristics of patients in various settings were identified from the literature search. These studies were open prospective studies and aimed to evaluate the safety and efficacy of outpatient assisted withdrawal. Feldman and colleagues (1975) evaluated an outpatient treatment programme for alcohol withdrawal (n=564). The authors reported that only 47% required outpatient assisted withdrawal and 19% required inpatient assisted withdrawal. Outpatient assisted withdrawal was successful and had a low dropout rate of 14%. However, the authors attributed this success to the involvement of the family early on, the use of withdrawal medication and involvement in peer group therapeutic activity. The results of an earlier study reflected these findings (Alterman *et al*., 1988). The investigators reported that ambulatory assisted withdrawal was relatively successful for mild-to-moderate alcohol withdrawal symptomatology.

Soyka and Horak (2004) assessed the efficacy and safety of outpatient assisted withdrawal in a German open prospective study. Alcohol dependent participants were excluded if they presented with severe alcohol-related disorders, such as seizures or psychosis, or major psychiatric and medical comorbidity. Some participants referred to the treatment clinic had to be admitted for inpatient care (n=348) leaving 331 patients being treated in an outpatient setting. The study reported very high completion rates (94%) for patients in an outpatient assisted withdrawal programme. Furthermore, outpatient assisted withdrawal was associated with increased participation in further treatment (91% of initial sample). Soyka and Horak (2004) additionally found that of those who completed assisted withdrawal successfully, all entered either motivationally- or psychotherapy-based treatment.

Stinnett (1982) evaluated the effectiveness and safety of 116 participants referred for outpatient assisted withdrawal in an alcoholism treatment centre. Fifty percent completed treatment, and 89% of these completers went on to continue with follow-up rehabilitation treatment. Collins and colleagues (1990) assessed the efficacy of a UK-based outpatient alcohol withdrawal programme. Of those deemed suitable for outpatient assisted withdrawal (n=76; 44% of all referrals), 79% successfully completed the treatment. These patients were severely alcohol dependent (91% had an SADQ score greater than 30). However, not all studies have reported such favourable completion rates. For example, in a dependent sample of 26 patients (77% with a SADQ score greater than 31), Drummond and Chalmers (1986) reported that only 23% of patients completed assisted withdrawal and 19% attended a follow-up 1 month later.

In a UK-based RCT, Alwyn and colleagues (2004) evaluated the addition of a brief psychological intervention to GP-managed home-based assisted withdrawal. The psychological intervention consisted of five 30-minute sessions with motivational, coping skills and social support approaches. The study reported that both the control and the psychological intervention group (total n=91) showed significant improvements in drinking outcomes from baseline to follow-up (3- and 12-month) indicating that home-based assisted withdrawal was effective. In addition, the psychological intervention group showed significantly greater improvements than the control group at and 12 month follow-up. These results suggest that there is benefit in adding brief psychological intervention to assisted withdrawal.

5.25.5 Indications for inpatient treatment

Medical indicators for inpatient treatment

For the majority of people who misuse alcohol, outpatient or home-based assisted withdrawal appears to be safe, viable and effective (see above). However, for a minority of patients, a non-residential setting for assisted withdrawal may be inappropriate or unsafe. An inpatient setting may be more appropriate for the management of moderate to severe withdrawal symptoms such as DTs and seizures, chronic comorbid medical, surgical and psychiatric problems (for example, suicidal ideation), pregnancy, or if the patient is not able to take medication by mouth (Bischof *et al*., 2003; Blondell *et al*., 2002; Blondell, 2005; Dukan *et al*; 2002; Ferguson *et al*., 1996; Kraemer 1997; Saitz & O'Malley, 1997;). There is evidence to suggest that a history of multiple prior episodes of assisted withdrawal may lead to an increased risk of seizures and withdrawal problems (Booth & Blow, 1993; Brown *et al*., 1988; Lechtenberg & Worner, 1990), and so a number of previous unsuccessful attempts at outpatient assisted withdrawal may also suggest the need for referral to inpatient setting. Dependence on drugs can increase the risks associated

with withdrawal and also the duration and severity of withdrawal symptoms, therefore patients with comorbid drug misuse disorders may require treatment in an inpatient setting. Research suggests that older patients (aged 60 years and above) are more at risk of cognitive and functional impairment during withdrawal and hence should be considered for inpatient care (Kraemer, 1997).

Other indicators for inpatient treatment

Concomitant medical need or the potential for medical complications are not the only factors that need to be taken into account when considering assisted withdrawal in an inpatient setting. Pettinati and colleagues (1993) found that those with high psychiatric comorbidity and/or poor social support benefited more from inpatient than outpatient treatment. Homeless patients requiring assisted withdrawal may also require inpatient care unless other shelter and accommodation can be arranged. For example, in a large study assessing the effectiveness of an ambulatory assisted withdrawal programme in the Veterans Administration system in the US (Wiseman *et al*., 1997), half of the patients were homeless. The study reported that 88% of patients successfully completed assisted withdrawal and 96% of these successful completers were referred for further treatment on either an inpatient or an outpatient basis. However, the programme provided supported housing for the homeless during the period of assisted withdrawal. Although low socioeconomic status and homelessness may make outpatient assisted withdrawal more challenging, they are not necessarily contraindications for treatment failure and hence should be assessed on a more detailed individual basis. O'Connor and colleagues (1991) reported that socially disadvantaged people were not at an increased risk of unsuccessful assisted withdrawal in an outpatient setting.

From the patients' perspective, it has been suggested that gains made in inpatient assisted withdrawal may not be easily transferable to the patient's home and social environment (Bischof *et al*., 2003). Undertaking assisted withdrawal in a home or outpatient setting enables the patient to retain important social contacts that may facilitate their attempts to achieve abstinence as well as subsequent rehabilitation. Patients can continue in employment (if appropriate) and be in a familiar environment with family support, which may help to minimise stress and anxiety and help to motivate them. It has also been suggested that the home environment is also less stigmatising than an inpatient setting for assisted withdrawal (Allen *et al*., 2005). In an interesting study assessing patients' perceptions and fears of alcohol withdrawal, Allen and colleagues (2005) found that patients were fearful and concerned about the psychiatric residential setting for assisted withdrawal and expressed feelings of stigmatisation associated with being in an 'institutional' setting. The authors also reported no difference in patient satisfaction between a home and outpatient setting for assisted withdrawal. Additionally, patient satisfaction with outpatient assisted withdrawal services have also been found to be high when administered in an intensive day programme (Strobbe *et al*., 2004). Stockwell and colleagues (1990) found that three-quarters of patients preferred their home as the setting for assisted withdrawal, and two-fifths and one-third were unwilling to undergo withdrawal in, respectively, a psychiatric hospital and a general hospital. The patients also emphasised the importance of support from the nurse supervising their assisted withdrawal, the breathalyser, medications, telephone support service and the involvement of supporters, familiar surroundings, privacy and confidentiality, and being able to stay with their family.

Another factor that may be relevant to the provision of home or outpatient assisted withdrawal is availability of treatment capacity. An early report (Stockwell *et al*., 1986) revealed that in the

Exeter Health Authority, GPs arranged as many home-based assisted withdrawals as hospital-based. However, of the home-based assisted withdrawals, two-fifths were unsupervised. Approximately a third of GPs were reluctant to take medical responsibility for home-based assisted withdrawal, but of those who were happy to, they reported a preference for this setting. Winters and McGourty (1994) also surveyed GPs in Chester and Ellesmere Port. Approximately 60% reported that they provided home-based assisted withdrawal from their practices. However, 10% believed specialist help was required. Additionally, they reported that unsuccessful home-based assisted withdrawal was usually due to lack of support at weekends and lack of patient motivation. Over 20% of Northumberland GPs reported carrying out home-based assisted withdrawals in the last year (Kaner & Masterson, 1996). Similar to McGourty (1994), most GPs stressed the importance of having daily supervision as well as more information about the process of assessing patients for suitability for home-based assisted withdrawal.

Inappropriate admission for residential assisted withdrawal

In services with ready access to inpatient facilities for assisted withdrawal, there is evidence to suggest that given the likelihood of medical complications more patients are admitted than is necessary. Whitfield (1982) reported than only 5% of people with alcohol problems require hospitalisation for withdrawal management. Booth and colleagues (1996) assessed appropriate and inappropriate utilisation of inpatient services for assisted withdrawal for alcohol in the US. The study, which randomly sampled a number of patients admitted into Veterans Administration medical centres, found that only 16% of alcoholics undergoing inpatient assisted withdrawal were appropriately admitted, and that the majority of these had medical or neurological complications such as liver cirrhosis, chest pains, kidney failure, gastrointestinal bleeding and seizures, and therefore met admission criteria. However, 84% were admitted for the purpose of monitoring alone and did not meet Appropriateness Evaluation Protocol (AEP) criteria for inpatient admission. Furthermore, the majority of inappropriately admitted patients did not develop any serious complications that could have justified inpatient care. These patients had lengthy admission length of 11 days on average, which has serious cost implications. An earlier study (Booth *et al*., 1991) also reported similar findings, albeit with a higher percentage (55%) of appropriate admissions.

The implementation of a standardised policy that guides the decision about inpatient admission or outpatient assisted withdrawal in a small community hospital resulted in a significant reduction in the number of admissions (Asplund *et al*., 2004). Furthermore, no patients needed hospitalisation for withdrawal complications, which indicates that outpatient assisted withdrawal is safe for the majority of patients without prior complications as identified by a thorough assessment. Outpatient assisted withdrawal may be more appropriate for a population with less severe problems. In a sample of male military veterans enrolled in outpatient withdrawal, Webb and colleagues (1988) reported that 54% successfully completed outpatient assisted withdrawal, 22% were admitted for inpatient care and 24% dropped out of the treatment. The group referred for inpatient care had a significantly higher level of dependence (measured by SADQ score) than those who successfully completed outpatient assisted withdrawal. This would suggest that inpatient assisted withdrawal may be more appropriate for patients with more severe alcohol dependence.

5.25.6 Health economics evidence

Systematic literature review

The literature search identified only one economic study that assessed the cost effectiveness of different settings for assisted withdrawal (Parrott *et al.,* 2006). The study evaluated two UK-based withdrawal programmes for people dependent on alcohol. The first intervention was a 10-day assisted withdrawal in a 22-bed facility in Manchester staffed by mental health nurses with support from a local GP. The second intervention was a brief hospitalisation programme based at a Newcastle NHS facility. This involved 3-day inpatient assisted withdrawal, if required, followed by attendance at a day programme. Both programmes were compared with no intervention rather than with each other because baseline data was compared with clinical and economic outcome data collected at 6 months after implementation. The economic analysis adopted a societal perspective. It included costs to the NHS, other alcohol treatment services, social services and the criminal justice system. The outcome measures used were QALYs for the cost-utility analysis and unit of drink reduction per day or reduction in percentage of drinking days in the cost-effectiveness analysis. QALYs were estimated using EQ-5D scores obtained from participants in the study.

In the cost-effectiveness analysis, the cost per unit reduction in alcohol was £1.87 in the Manchester sample and £1.66 in the Newcastle sample. The cost per reduction of one drink per day was £92.75 in the Manchester sample and £22.56 in the Newcastle sample. The cost per percentage point reduction in drinking was £30.71 in the Manchester sample and £45.06 in the Newcastle sample. In the cost-utility analysis, the cost per QALY gained was £65,454 (£33,727 when considering only treatment costs) in the Manchester sample and £131,750 (£90,375 treatment costs only) in the Newcastle sample. Overall, the authors concluded that both alcohol withdrawal programmes improved clinical outcomes at a reasonable cost to society. The validity of the study results is limited by the absence of a non-treatment group for both alcohol withdrawal programmes as changes in clinical outcomes may have occurred without the interventions. Also, the study design meant that time-dependent confounding variables could not be controlled for. Data for each programme were collected from single centres, which may limit generalisability of the study findings to other UK centres. The small patient sample size in both centres and substantial loss to follow-up also limits the robustness of the analysis. It should be noted that patients in the two centres were different in terms of severity of dependence, the number and severity of alcohol-related problems, and socioeconomic status, and therefore direct comparison of costs and outcomes associated with each intervention is not appropriate.

Summary of existing economic evidence

The findings of Parrott and colleagues (2006) suggest that both programmes may be cost effective in terms of reduction in alcohol consumption rather than QALYs gained. The settings, the costs reported and the measure of benefit adopted in the study make this study directly applicable. However, the effectiveness evidence is not without limitations: the comparator of no treatment may not be relevant and the robustness of the results was not fully explored in sensitivity analyses.

Cost minimisation analysis of assisted withdrawal in different settings

The cost effectiveness of assisted withdrawal across different settings was considered by the GDG as an area with potentially significant resource implications. As previously discussed, clinical evidence was derived from studies with different designs and therefore it was not possible to synthesise the clinical data in order to conduct a formal economic evaluation.

Nevertheless, existing clinical evidence suggests that the effectiveness of home-based or outpatient assisted withdrawal attempted in outpatient/home settings is similar to that of assisted withdrawal provided in inpatient/residential settings. Therefore, a simple cost-minimisation analysis was undertaken to estimate costs associated with assisted withdrawal that are specific to the setting in which assisted withdrawal is provided.

Three different assisted withdrawal settings were considered in the cost-minimisation analysis: inpatient/residential, outpatient and home-based. The healthcare resource use estimates for each setting were based on descriptions of resource use in studies included in the systematic literature review of clinical evidence. Information was mainly sought in studies conducted in the UK, as clinical practice and respective resource use described in these studies is directly relevant to the guideline context. After reviewing the relevant literature, it was decided to utilise resource use estimates reported in Alwyn and colleagues (2004), which were then adapted according to the expert opinion of the GDG in order to reflect current routine clinical practice within the NHS. The estimated resource use was subsequently combined with national unit costs in order to provide a total cost associated with provision of assisted withdrawal in the three settings assessed. Unit costs were derived from national sources (Curtis, 2009; DH, 2010) and reflected 2009 prices. It should be noted that the cost estimates reported below do not include the cost of drugs administered to people undergoing assisted withdrawal. However, this cost is common to all assisted withdrawal settings and therefore its omission does not affect the relative costs between different settings.

Inpatient/residential assisted withdrawal

According to Alwyn and colleagues (2004), inpatient/residential assisted withdrawal lasts 2 weeks and requires an extra outpatient visit. The GDG estimated that inpatient assisted withdrawal may last longer, between 2 and 3 weeks. The unit cost of NHS adult acute mental health inpatient care is £290 per patient day (DH, 2010). The unit cost of hospital outpatient consultant drug and alcohol services is £85 per face-to-face contact for a follow-up visit (DH, 2010). By combining the above resource use estimates with the respective unit costs, the total cost of inpatient/residential assisted withdrawal is estimated to range between £4,145 and £6,175 per person treated.

Outpatient assisted withdrawal

Outpatient assisted withdrawal is estimated to require six outpatient attendances (Alwyn *et al*., 2004). The unit cost of a face-to-face contact with hospital outpatient consultant drug and alcohol services is £181 for the first visit and £85 for each follow-up visit (DH, 2010). By combining these data, the total cost of outpatient assisted withdrawal is estimated at £606 per person treated.

Home-based assisted withdrawal

Alwyn and colleagues (2004) estimated that home-based assisted withdrawal requires six community psychiatry nurse (CPN) home visits, lasting 30 minutes each. The GDG were of the opinion that the first of these visits should be replaced by an outpatient visit to alcohol consultant services, so that appropriate assessment is carried out before starting assisted withdrawal. Moreover, the GDG advised that the travel time of the healthcare professional providing home-based assisted withdrawal should be taken into account. Considering that home visits often take place in remote areas, the GDG estimated that the travelling time of the healthcare professional staff was likely to range between 1 and 2 hours per home visit. The unit

cost of a face-to-face contact with outpatient consultant drug and alcohol services is £181 for the first visit (DH, 2010). The unit cost of a CPN is not available for 2009. The total cost of home-based assisted withdrawal was therefore based on the unit cost of community nurse specialists (Band 6), as this type of healthcare professional is expected to provide home-based assisted withdrawal. The unit cost for community nurse specialists is £35 per working hour and £88 per hour of patient contact (Curtis, 2009). This unit cost includes salary (based on the median full-time equivalent basic salary for Agenda for Change Band 6 of the January to March 2009 NHS Staff Earnings estimates for qualified nurses), salary oncosts, capital and revenue overheads, as well as qualification costs. The unit cost per working hour was combined with the estimated travelling time, while the unit cost per hour of patient contact was combined with the estimated total duration of home visiting. A £4 travel cost was assumed for each visit. By combining all the above data, the total cost of home-based assisted withdrawal was estimated to range between £596 and £771.

Summary

The cost-minimisation analysis indicates that, provided that the different assisted withdrawal settings have similar effectiveness, then outpatient and home-based assisted withdrawal are probably more cost effective than inpatient assisted withdrawal, resulting in an estimated cost saving of approximately £3,400 to £5,600 per person treated.

5.25.7 Clinical and health economic evidence summary

The evidence indicates that a community setting for assisted withdrawal is as effective and safe for the majority of patients as an inpatient or residential assisted withdrawal as long as the patient is without serious medical contraindications. It is also likely to be more cost effective as cost savings of between £3,400 to £5,600 per person may be generated The evidence reviewed is limited as there is only one RCT, but it should be noted that it is extremely difficult to undertake an RCT in this area given the clinicians concerns about the relative safety for more severely dependent patients. The GDG (drawing on the evidence in the reviews conducted for this guideline) therefore thought it important to consider the following factors when determining whether a community or residential/ inpatient assisted withdrawal is the most appropriate:

- a history of epilepsy or withdrawal-related seizures or DTs during previous assisted withdrawals
- a significant psychiatric or physical comorbidity (for example, chronic severe depression, psychosis, malnutrition, congestive cardiac failure, unstable angina, chronic liver disease)
- a significant learning disability
- significant cognitive impairment
- homelessness
- pregnancy
- older age

5.26 Evaluating dosing regimes for assisted withdrawal

5.26.1 Introduction

This section assesses the safety, efficacy, cost effectiveness and patient satisfaction associated with different medication regimens used in assisted withdrawal from alcohol. When undertaking assisted withdrawal, the patient is required to stop alcohol intake abruptly, and its effects are replaced by medication that has cross-tolerance. Once this process is achieved, the medication can be reduced at a rate that prevents withdrawal symptoms but without promoting over-sedation, and ultimately stopped altogether. Key elements of the process are to provide a large enough initial dose to prevent severe withdrawal symptoms including seizures, DTs, severe anxiety or autonomic instability, but to withdraw the medication before physical dependence on its effects begins.

5.26.2 Definitions of dosing regimen methods

Fixed-dose regimen

A fixed dose regimen involves starting treatment with a standard dose, not defined by the level of alcohol withdrawal, and reducing the dose to zero typically over 7 to 10 days according to a standard protocol.

Symptom-triggered regimen

A symptom-triggered approach involves tailoring the drug regimen according to the severity of withdrawal and complications the patient is displaying. The patient is monitored on a regular basis and pharmacotherapy is administered according to the patient's level of withdrawal symptoms. Pharmacotherapy only continues as long as the patient is displaying withdrawal symptoms and the administered dose is also dependent on the assessed level of alcohol withdrawal. Withdrawal symptoms are usually assessed by clinical experience and questioning the patient and/or with the use of a validated withdrawal measurement tool such as the Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar; Sullivan *et al.*, 1989).

Front-loading regimen

A front-loading regimen involves providing the patient with an initially high dose of pharmacotherapy and then using either a fixed dose or symptom-triggered dosing regimen for subsequent assisted withdrawal.

5.26.3 Aim of review and review protocol

As stated above, this section is concerned with the safety, efficacy, cost effectiveness and patient satisfaction different dosing regimens for assisted withdrawal and their appropriateness in various treatment settings. Furthermore, this section aims to evaluate medication for assisted withdrawal that is not appropriate or safe in a setting without 24-hour monitoring. The GDG identified that there would be insufficient RCT literature available to answer the clinical question, therefore it was decided by consensus to include all available studies in a systematic review using a narrative synthesis of the evidence. The review team assessed the literature identified from the search conducted by the NICE guideline on management of alcohol-related physical complications (NICE, 2010b); full details of the search strategies can be found in that

guideline. Studies were considered for inclusion in the narrative synthesis if they met the inclusion criteria (see Chapter 3) and if the population being assessed in the study reflected the scope of this guideline (see Appendix 1). Furthermore, studies were considered for inclusion in the narrative synthesis using the clinical review protocol described in Table 2. The outcomes of interest would indicate the efficacy (management of alcohol withdrawal syndrome, duration of treatment and amount of medication required), safety (development of complications), as well as patient and physician satisfaction of the dosing regimens.

Table 20: Clinical review protocol for the evaluation of different dosing regimens for assisted withdrawal from alcohol

Electronic Databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO; see the NICE guideline (NICE, 2010b) on management of alcohol-related physical complications for search strategies
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs; Systematic reviews;
Patient population	Adults (>18 years); Patients with alcohol withdrawal syndrome
Critical Outcomes	Main outcomes: severity of withdrawal; duration of treatment; total amount of medication; incidence of seizures and DTs or other complications Other outcomes: patient and physician satisfaction; completion rates

In addition the review team conducted a search for studies which evaluated patient indication for inpatient assisted withdrawal. The review team also reviewed the safety of using different types of medication for assisted withdrawal in a setting that does not have 24-hour monitoring. Due to the nature of the review question, the GDG identified that there would be a lack of RCT literature (confirmed by the original RCT search for this guideline) and hence a search was conducted for systematic reviews. The review team assessed the available literature identified from the search conducted by the NICE guideline on management of alcohol-related physical complications (NICE, 2010b).

5.26.4 Studies considered

Twelve studies evaluating the efficacy and safety of different regimens for assisted withdrawal were identified. Nine of these studies compared a symptom-triggered (ST) regimen of administering alcohol withdrawal medication (with or without front-loading) to a fixed-dosing (FD) regimen (Saitz *et al*., 1994; Weaver *et al*. 2006; Manikant *et al*., 1993; Sullivan *et al*., 1991; Daeppen *et al*., 2002; Day *et al*., 2004; Wasilewski *et al*., 1996; Lange-Asschenfeldt *et al*., 2003; Hardern and Page., 2005), and three studies compared usual non-protocol routine based hospital care to a ST regimen (DeCaroulis *et al., 2007;* Reoux and Miller, 2000; Jaeger *et al*., 2001). The characteristics and settings of the included studies can be found in Table 21.

Table 21: **Characteristics of studies evaluating dosing regimen methods**

Study	Study design	Setting	Comparison	Method of assessing alcohol withdrawal syndrome
Daeppen2002	Randomised placebo controlled trial	Inpatient alcohol treatment unit	1. ST (n=56) 2. FD (n=61)	CIWA-Ar administered half an hour after placebo dose
Day2004	RCT	Inpatient alcohol treatment unit	1. ST front loading (n=11) 2. FD (n=12)	CIWA-Ar administered every 90 minutes
DeCarolis2007	Retrospective audit	Inpatient intensive care unit (Veterans Administration medical centre)	1. ST (n=21) 2. Routine hospital FD (n=16)	Minnesota Detoxification Scale (MIND)
Hardern2005	Retrospective audit	General hospital inpatient ward	1. ST (n-23) 2. Regular dosing (n=28)	CIWA-Ar (when administered not reported)
Jaeger2001	Retrospective chart analyses	General hospital inpatient ward	1. ST (n=84) 2. Usual Care: FD or as needed at discretion of medical staff (n=132)	CIWA-Ar administered every 1 to 2 hours
Lange-Asschenfeldt2003	Retrospective chart analysis	General hospital inpatient ward	1. ST (n=33) 2. FD (n=32)	Modified German CIWA-Ar administered at: nitial assessment; irst day of admission and days 1 to 3 (every 2 hours); days 4 and 5 (every 4 hours); day 6 (4 times daily); day 7 (three times daily); days 8 and 9 (twice daily)
Manikant1993	RCT	Psychiatric inpatient ward	1. ST front loading (n=20) 2. FD (n=21)	CIWA-Ar administered every 90 minutes
Reoux2000	Retrospective chart analysis	ST = Inpatient specialist alcohol unit (Veterans Administration medical centre); Routine care = General Medical Ward or Inpatient psychiatry unit	1. ST (n=26) 2. Routine hospital alcohol withdrawal practice (varied and non-protocol based) (n=14)	CIWA-Ar administered 1 hour after being medicated
Saitz1994	Randomised placebo controlled trial	Inpatient specialist alcohol unit (Veterans Administration medical centre)	1. ST (n=51) 2. FD (n=50)	CIWA-Ar administered hourly
Sullivan1991	Retrospective case series	General hospital inpatient ward	1. ST front loading (n=133) 2. FD front loading (n=117)	CIWA-Ar administered hourly and then as needed (clinical judgement)
Wasilewski1996	Prospective cohort	Psychiatric inpatient ward	1. ST front loading (n=51) 2 FD (n=45)	CIWA-Ar administered every 1 to 2 hours
Weaver2006	Quasi-randomised	General hospital inpatient ward	1. ST (n=91) 2. FD (n=92)	CIWA-Ar at initial assessment and then every 4 hours

Table 22: Summary of findings of studies evaluating dosing regimen methods

Study	Outcomes	Results
Daeppen2002	Total amount of medication required	ST (95.4 [107.7] mg) significantly less than FD (231.4 [29.4] mg) (Mann-Whitney *U* = 5.84; p<0.001)
	Number using medication	ST (39.3%) significantly fewer patients than FD (100%) ($\chi 2$ = 52.2; p<0.001)
	Duration of treatment	Sub-group analyses (n=19) with history of complications: ST (22.7 [26.68] hours) significantly shorter than FD (62.1 [6.18] hours) (Mann-Whitney *U* = 2.87, p=0.004)
	Patient well-being	No significant difference between groups in health concerns, anxiety, energy or depression
	Incidence of complications	No significant difference in number of seizures, hallucinations or DTs
Day2004	Total amount of medication required	ST (222 mg) significantly less than FD(700 mg) (p<0.001)
	Duration of treatment	ST (8 hours) significantly shorter than FD (242 hours) (p<0.001)
	Severity of alcohol withdrawal	No significant difference between groups
	Incidence of complications	No significant difference between groups
	Patient satisfaction	No significant difference in self-perceived adverse symptoms or patient satisfaction with regimens
DeCaroulis2007	Time to reach symptom control	ST (7.7 [4.9] hours) significantly shorter time than routine FD (19.4 [9.7]) (p=0.002)
	Total amount of medication required	ST (1044 [534] mg) significantly less than routine FS (1677 [937]) (p=0.014)
	Duration of treatment	No significant difference between groups
Hardern2005	Total amount of medication required	No significant difference between groups
	Duration of treatment	No significant difference between groups
	Time from first to last administration	ST (48 hours) significantly shorter than regular dosing (110 hours) (p=0.086)
Jaeger2001	Duration of treatment	No significant difference between groups
	Total amount of medication required	No significant difference between groups
	Incidence of complications	No significant difference in incidence of complications overall; ST had significantly less incidence of DTs (p=0.04) (ST = 20.5%; Usual care = 6.9%)
Lange-Asschenfeldt2003	Total amount of medication required	ST (median 4352 [4589]) significantly less than FD (median 9921 [6599]) (p=0.0004)
	Duration of treatment	ST (median 4.2 [2.9]) significantly less than FD (median 7.5 [3.3]) (p=0.0003)
	Incidence of complications	No significant difference between groups
	Use of co-medication	No significant difference between groups
Manikant1993	Total amount of medication required	No statistical data provided: ST = 67 mg; FD = 200 mg
	Severity of alcohol withdrawal	No significant difference between groups

Study	Outcomes	Results
Reoux2000	Total amount of medication required	ST (82.7 [153.6]mg) significantly less than routine practice (367.5 [98.2]mg) (p=0.004)
	Number of doses required	ST (1.7 [3.1]) significantly less than routine practice (10.4 [7.9]) (p=0.001)
	Duration of medication use	ST (10.7[20.7]) significantly less than routine practice (64.3[60.4]) (p=0.006)
	Adverse effects	None present in both groups
Saitz1994	Duration of treatment	ST (median = 9 hours) significantly shorter than FD (median 68 hours) (Wilcoxon z =5.68; p<0.001)
	Total amount of medication required	ST (100 mg) significantly less than FD (425 mg) (Wilcoxon z = 5.30, p<0.001)
	Severity of alcohol withdrawal	No significant difference between groups (p=0.73)
	Incidence of complications	No significant difference between groups in incidence of DTs (p=0.36); hallucinations (p=0.62); seizures (none); lethargy (p=0.42); leaving the hospital against medical advice (p=0.68); readmission within 30 days (p=0.72)
	Participation in further rehabilitation treatment after assisted withdrawal	ST (69%) greater than FD (50%) (non-significant) (p=0.06)
Sullivan1991	Total amount of medication required	ST (50 mg) significantly less than FD (75 mg) (p=0.04)
	Duration of treatment	No significant difference between groups
	Number of patients requiring <20 mg of medication	ST (33%) significantly more than FD (12.8%) (p=0.05)
	Rate of discharge against medical advice	No significant difference between groups
	Rates of complication	No significant difference between groups
Wasilewski1996	Total amount of medication required	SD (87 [47.2] mg) significantly less than FD (1784 [1800] mg) (p<0.00001)
	Duration of delirium	ST (6.9 [4.8]) significantly less than FD (33.8 [25.7]) (Mann-Whitney U = 265.0, p<0.001)
	Abnormalities and somatic disorders	No significant difference between groups
Weaver2006	Total amount of medication required	ST (29 mg) significantly less than FD (100 mg) (p<0.0001)
	Severity of alcohol withdrawal	No significant difference between groups in first 2 days
	Protocol errors	ST (17.6%) significantly more than FD (7.6%) ($\chi 2$ = 4.14; p=0.042)

5.26.5 Narrative summary of findings

Medication use and duration of treatment

The results of most studies favoured the use of ST over FD regimens for outcomes assessing medication use and duration of treatment (see Table 4). The ST approach resulted in lower medication needed (Daeppen *et al*., 2002; Day *et al*., 2004; DeCarolis *et al*., 2007; Lange-Asschenfeldt *et al*., 2003; Reoux & Miller, 2000; Saitz *et al*., 1994; Sullivan *et al*., 1991; Wasilewski *et al*., 1996; Weaver *et al*. 2006), lower frequency of administration (Daeppen *et al*., 2002; Reoux & Miller, 2000), and a shorter duration of treatment (Daeppen *et al*., 2002; Day *et al*., 2004; Lange-Asschenfeldt *et al*., 2003; Reoux & Miller, 2000; Saitz *et al*., 1994;). However, not all studies assessing these outcomes reported results favouring an ST approach. Sullivan and colleagues (1991) and Jaeger and colleagues (2001) found no difference between ST front loading and FD front loading regimens in terms of length of stay, and Jaeger and colleagues (2001) reported no significant difference between groups in total dose of medication required. Hardern and Page (2005) found no difference in dose administered and length of stay between ST and regular FD regimens.

Severity of withdrawal symptoms

DeCarolis and colleagues (2007) reported significantly less time to reach symptom control in the ST protocol group when compared with an FD regimen. Saitz and colleagues (1994) found no difference between an ST and FD regimen in time taken from admission to achieving a CIWA-Ar score of less than 8. Manikant and colleagues (1993) and Day and colleagues (2004) also found no significant difference in severity of withdrawal (using the CIWA-Ar) between an ST front loading and an FD regimen.

Rates of complications or adverse effects

Jaeger and colleagues (2001) reported significantly fewer episodes of DTs in the ST regimen group when compared with routine care but found no difference in overall complication rates. Other studies, however, reported no difference between ST and other FD regimens/routine care in rates of complications and adverse effects (for example, incidence of seizures, DTs and hallucinations) (Lange-Asschenfeldt *et al*., 2003; Reoux and Miller, 2000; Saitz *et al*., 1994; Sullivan *et al*., 1991). In Wasilewski and colleagues' (1996) study, although patients in the ST front loading group had a significantly shorter duration of delirium than the FD group, no significant difference was observed in somatic disorders and abnormalities. Additionally, Day and colleagues (2004) did not find a significant difference between ST front loading and FD regimens in self-reported adverse symptoms.

Other outcomes

Other outcomes, including patient satisfaction, discharge against medication advice, use of co-medication and protocol errors, were reported in the reviewed studies. Daeppen and colleagues (2002)[20] and Sullivan and colleagues (1991) reported that there were no significant differences in patient comfort level between groups, and Day and colleagues (2004) reported no significant difference between ST front loading and FD regimens in terms of patient satisfaction. Two studies (Sullivan *et al*., 1991; Saitz *et al*., 1994) reported no difference between ST and FD regimens in terms of rates of discharge against medical advice, and Lange-Asschenfeldt and

[20] In Daeppen and colleagues' (2002) study, 60.3% of patients did not require pharmacological assisted withdrawal.

colleagues (2003) found no difference in use of co-medication. Weaver and colleagues (2006) reported significantly more protocol errors in the ST group as opposed to the FD regimen group.

Symptom-triggered assisted withdrawal in a general medical setting

The studies reviewed above are probably not reflective of patients with complex problems who typically are admitted to a general hospital ward for medical treatment but present with withdrawal symptoms, that is, they are undergoing unplanned withdrawal (Hecksel *et al*., 2008). For example, although the Jaeger and colleagues' (2001) study found fewer episodes of DTs in the ST regimen group, patients were excluded from the study if they presented with medical comorbidities. In a general admissions unit, this in effect would exclude any post-surgical patients (Hecksel *et al*., 2008). Additionally, Reoux and Miller (2000) excluded any patients with complex medical histories, and Sullivan and colleagues (1991) did not take into account medical comorbidity in their discussions. Therefore, Hecksel and colleagues (2008) suggest that in these studies, which have assessed an ST approach in a non-specialist general medical setting, patients that are most likely to develop complications such as DTs have not been investigated using the CIWA-Ar tool and therefore some uncertainly about its value with this population remain (Ferguson *et al*., 1996).

The majority of the ST studies were conducted in addiction specialist inpatient settings or psychiatric hospitals, which have highly trained specialist staff familiar with the ST dosing regimen and methods (Daeppen *et al*., 2002; Day *et al*., 2004; Lange-Asschenfeldt *et al*., 2003; Manikant *et al*., 1993; Reoux & Miller, 2000; Saitz *et al*., 1994; Wasilewski *et al*., 1996). When dosing regimens were compared in non-alcohol specialist settings, that is, in general hospital medical wards, extensive training was delivered to staff (Jaeger *et al*., 2001; Sullivan *et al*., 1991; Weaver *et al*., 2006). For example, in the Sullivan study, training was delivered over a 6-month period with the assistance of clinical nurse specialist in alcohol and substance misuse. In the Hardern (2005) study a retrospective audit compared the use of an ST regime (which had been introduced in the medical admissions unit) with regular fixed dosing. However, nurses who were trained to use the scoring tool were frequently unavailable when the patient was admitted. This is reflective of the competing demands on staff in a non-addiction treatment setting. This variability can also be observed in different non-specialist departments such as emergency departments (Kahan *et al*., 2005).

Nurses, whether in a specialist unit, psychiatric ward, general medical ward, or in the community, play a vital role in successful assisted withdrawal. Stockwell (1990) found both patients and family members rated the support from community nurses as more important than medication for assisted withdrawal. Nursing staff in specialist addiction treatment centres are highly skilled and trained in all aspects of the medical management of alcohol withdrawal (Cooper, 1994) and have a working knowledge of current working practices and liaise with other staff and services (Choudry, 1990). This may well have an impact on the efficacy of the ST programmes in the studies above.

Most physicians and nurses working in general medical wards are not specialists in the management of alcohol dependence. This is a concern as the first point of contact for many alcohol dependent people is not a specialist addiction unit, but usually a general physician in a non-specialist treatment setting such as a general medical ward (O'Connor *et al*. 1998). Nurses in general medical practice may also lack specialised knowledge and education about addiction

and assisted withdrawal (Coffey, 1996; Happell & Taylor, 1999; Ryan & Ottlinger, 1999). Even if training were provided, the obstacles to ensuring comprehensive training in a general medical setting also needs consideration (Schmacher *et al*., 2000).

Bostwick and Lapid (2004) reported on the use of a symptom-triggered approach by psychiatrists at the Mayo Clinic in Rochester, Minnesota. A CIWA-Ar controlled protocol was not effective in managing alcohol withdrawal and patients deteriorated with use of an ST approach. In these specific cases reported by Bostwick and Lapid (2004), patients were assumed to be presenting with pure alcohol withdrawal syndrome. However, as no thorough clinical interview was utilised and the patients could not communicate effectively, medical staff did not ascertain whether the apparent alcohol withdrawal symptoms presented were a result of other acute medical conditions such as sepsis, pain and shock. In another study of admissions in Mayo Clinics, Hecksel and colleagues (2007) found that half of patients receiving ST assisted withdrawal did not meet criteria using the CIWA-Ar. The investigators reported that 44% of patients given this protocol had not been drinking, and 23% were unable to communicate effectively. Surprisingly, of those who could communicate, 64% were not currently drinking and were still receiving ST medication. Again, and reflective of Bostwick and Lapid's (2004) study, medical histories were overlooked by physicians with a slight hint at alcohol use in the patient's history informing a decision to use this approach. Physicians also regularly assumed that automatic hyperactivity and psychological distress were a result of alcohol withdrawal and hence a high CIWA-Ar score was attained, resulting in unnecessary benzodiazepine treatment. The investigators concluded that in patients with a history of alcohol dependence who are likely to develop adverse effects (DTs and seizures), a CIWA-Ar based ST approach is not appropriate and a more patient-centered, personalised approach to medication management that goes beyond the CIWA-Ar is needed. Furthermore, in medical and surgical patients with a history of drinking, the ST approach to medication management has not been proven. Bostwick and Lapid (2004) and Hecksel and colleagues (2007) also conclude that an ST approach is not appropriate for patients with complex medical and surgical comorbidities and hence may not be suitable for many patients presenting with alcohol withdrawal syndrome in a general medical setting.

Medication not appropriate for use in a setting without 24-hour monitoring

The use of certain medications for assisted withdrawal may not be appropriate in non-residential settings such as an outpatient clinic or the patient's home. Outpatient medication should be administered orally, have low potential for misuse or overdose, and have few side effects (O'Connor *et al*., 1994).

Contraindications for benzodiazepines and chlormethiazole in non-residential settings identified in the literature are set out below.

Benzodiazepines

Although long-acting benzodiazepeines (such as chlordiazepoxide and diazepam) are preferred for patients with alcohol withdrawal syndrome, short-acting benzodiazepeines (such as oxazepam) may be preferred in those for whom over-sedation must be avoided, in people with liver disease who may not be able to metabolise long-acting agents efficiently, and in people with chronic obstructive pulmonary disease (COPD) (Blondell, 2005; Mayo-Smith *et al*., 2004). However, apart from patients with liver failure and those with COPD (who may well be managed as inpatients [see above]), short-acting benzodiazepeines may not be suitable for outpatient assisted withdrawal due to the risk of breakthrough seizures (Mayo-Smith, 1997).

Furthermore, rapid-acting benzodiazepeines (such as diazepam, alprazolam and lorazepam) may have a greater potential for misuse than slower-acting benzodiazepeines such as chlordiazepoxide, oxazepam and halazepam (Griffiths & Wolf, 1990; McKinley, 2005; Soyka & Horak, 2004).

Chlormethiazole

Chlormethiazole is used in inpatient care as it has a short half-life (Majumdar, 1990). However, it requires close medical supervision and is therefore not recommended for non-residential settings such as outpatient clinics, patients' homes and prisons. Furthermore, it is addictive (although this is unlikely to develop in the short time period of an assisted withdrawal) and, more importantly, it can have fatal consequences in overdose resulting from coma and respiratory depression, especially when taken with alcohol (Gregg & Akhter, 1979; Horder, 1978; McInnes *et al*., 1980; McInnes, 1987; Stockwell *et al*., 1986).

5.26.6 Assisted withdrawal in the prison setting

Research evaluating assisted withdrawal in custodial settings such as police custody and prison is scarce. Individuals taken into police custody are often under the influence of alcohol and some of these individuals may be alcohol dependent (Naik & Lawton, 1996). Deaths in UK police custody have been associated with alcohol intake (Yoshida *et al*., 1990) and 86% of fatalities in police custody are associated with recent alcohol consumption and alcohol dependence (Giles & Sandrin, 1990). However, there is little guidance on the assessment and management of alcohol withdrawal in police custody or prison settings but also evidence to suggest that any such guidance is not always followed (Ghodse *et al.,* 2006).

People received into prison carry a heightened risk of suicide in the early days of their custody; one third of all prison suicides happen within the first week of imprisonment (Shaw *et al* 2003). This phase coincides with alcohol withdrawal for around one in five prisoners, and the above study found an association between alcohol dependence and risk of suicide. Severity of dependence is commonplace among people entering prison: the last national study to be conducted found that 6% of all prisoners returned AUDIT scores of 32 and above (Singleton *et al*, 1997). (It should be noted that screening with AUDIT now forms part of the routine admission programme of the prison service). The break in consumption that begins with arrest means that many dependent people arrive in prison in active states of withdrawal. This position is further complicated by the high levels of comorbid drug (including opiates, benzodiazepines and cocaine) misuse in the prison population (Ramsay, 2003). Due to the increased risk of suicide, severity of dependence and developing withdrawal effects, clinical management of alcohol withdrawal should begin on the day of reception into custody. The preferred agent of assisted withdrawal in the prison service has been chlordiazepoxide (DH, 2006).

Following alcohol withdrawal, there is some evidence that alcohol treatment programmes addressing offending behaviour can reduce rates of re-offending (Hollis, 2007; McCulloch & McMurran, 2008), but these studies both lack a well-matched control group. A comparative study of a modified therapeutic community and a standard mental health intervention for the treatment of male prisoners with both mental health and substance misuse problems found evidence that the therapeutic community group re-offended at a significantly reduced rate (Sacks *et al*, 2004). Because alcohol is prohibited in prison, the majority of alcohol-dependent people will remain alcohol-free prior to their day of release.

5.26.7 Clinical evidence summary

There is some evidence to suggest that for assisted withdrawal, an ST regimen reduces medication use and duration of treatment and, therefore, is preferred in settings where 24-hour monitoring is available and the staff are highly trained in the use of this regimen. However, the evidence is not conclusive and some previous research has found no difference between ST and FD regimens in efficacy as well as for other outcomes such as rates of complication and patient experience. Furthermore, the studies that have evaluated this question are conducted in settings where 24-hour monitoring fro trained staff is available and in the majority of cases these are specialist addiction units and where this was not the case the staff involved in these studies were extensively trained (for periods up to six months) for the purpose of the study.

Due to the skill required to treat alcohol withdrawal with an ST regimen, there is a higher possibility of protocol errors where staff are not highly trained. This suggests that in a non-specialist inpatient setting, the ST approach may not be feasible, as staff in general medical settings may not the training, expertise and resources to conduct an ST regimen. Therefore, in non-specialist general settings, a tapered FD regimen may be more appropriate for assisted withdrawal.

There are currently no RCTs that assess the efficacy of an ST regimen for assisted withdrawal in an outpatient setting. This may be because the use of an inpatient or specialist ST dosing regimen in a community setting is unpractical as 24-hour or ad hoc monitoring is not achievable. The gradual tapering FD regimen is therefore more appropriate for outpatient assisted withdrawal as it involves providing medication according to a specified dose for a period of predetermined days. The medication dose is reduced until cessation. The evidence also indicates that chlormethiazole is not appropriate for use in outpatient assisted withdrawal because there is a high risk of misuse and overdose.

It is likely that some alcohol misusers taken into police custody may develop alcohol withdrawal syndrome. However, previous research suggests that alcohol withdrawal syndrome is not always detected in this setting. Staff should be aware of the importance of identifying possible alcohol withdrawal and be trained in the use of tools to detect alcohol dependence (for example, the AUDIT). Furthermore, due to the risk of suicide and medical complications that could develop from developing alcohol withdrawal, the management of alcohol withdrawal syndrome should occur immediately upon entry into custody.

5.27 From evidence to recommendations: assisted withdrawal

This section draws on the preceding two reviews of assisted withdrawal settings and drug regimens; the summaries of these reviews can be found in Sections 1.3.7 and 1.4.6.

The evidence indicated that a community setting for assisted withdrawal is as clinically effective and safe for the majority of patients as an inpatient or residential setting and it is also likely to be more cost effective. The GDG therefore decided that community-based assisted withdrawal should be the first choice for most patients. However, the GDG were aware that some of the more severe dependent patients, often with complex comorbidities, were often excluded from the studies reviewed. The GDG considered the literature that might inform this

issue and identified a number factors that would indicate that a residential or inpatient setting may be preferred to a community setting. They also considered which of the factors would suggest that assisted withdrawal should be managed in an inpatient setting with access to 24-hour specialist doctors and nurses with expertise in managing withdrawal in the context of significant comorbidity. The factors the GDG considered important are as follows:

- a history of epilepsy or withdrawal-related seizures or DTs during previous assisted withdrawals
- a significant psychiatric or physical comorbidity (for example, chronic severe depression, psychosis, malnutrition, congestive cardiac failure, unstable angina, chronic liver disease)
- a significant learning disability
- significant cognitive impairment
- a history of poor compliance and previous failed attempts
- homelessness
- pregnancy
- older age.

The review of drug regimens for assisted withdrawal drew on the NICE guideline on management of alcohol-related physical complications (NICE, 2010b) for both the initial review of the medication regimens and in order to ensure that there was a comprehensive and coherent approach to assisted withdrawal across both guidelines. The GDG was, therefore, concerned to build on the other guideline and develop recommendations that were feasible for use in a range of specialist settings in both inpatient, residential and community (including primary care) services. After carefully considering the evidence, the GDG came to the conclusion that symptom triggered assisted withdrawal was only practical in those inpatient settings that contained high levels of specially trained staff. They therefore took the view that the preferred method for assisted withdrawal was a fixed dose regimen for community and residential settings . In addition the GDG also considered how some of the complex comorbidities often encountered in specialist alcohol services may be best managed. In particular the GDG were concerned to provide advice on the management of comorbid alcohol, and benzodiazepine misuse. This was of concern as the GDG recognised the need to go above recommended BNF levels for people who were dually dependent in order to reduce the likelihood of seizures. In the absence of any evidence from the studies reviewed, the GDG reached agreement on this issue by informal consensus.

5.27.1 Recommendations

Interventions for assisted withdrawal

5.27.1.1 For service users who typically drink over 15 units of alcohol per day, and/or who score more than 20 on the AUDIT, consider:

- an assessment for and delivery of a community-based assisted withdrawal
- a referral to specialist alcohol services for further assessment and management if

there are safety concerns (see 5.27.1.3) about a community-based assisted withdrawal. **[KPI]**

5.27.1.2 Service users who need assisted withdrawal should typically be offered a community-based programme. Community-based programmes should vary in intensity between:

- an outpatient-based programme in which contact between staff and the service user averages 2–4 meetings per week over a 3-week period, and
- an intensive community programme in which the service user may attend a day programme lasting between 4 and 7 days per week over a 3-week period.

5.27.1.3 Consider inpatient or residential assisted withdrawal if the service user meets one or more of the following criteria. They:

- drink over 30 units of alcohol per day
- have a score of more than 30 on the SADQ
- have a history of epilepsy or experience of withdrawal-related seizures or delirium tremens during previous assisted withdrawal programmes
- need concurrent withdrawal from alcohol and benzodiazepines
- regularly drink between 15 and 20 units of alcohol per day and have:
  - significant psychiatric or physical comorbidities (for example, chronic severe depression, psychosis, malnutrition, congestive cardiac failure, unstable angina, chronic liver disease)
  - a significant learning disability or cognitive impairment.

Drug regimens for assisted withdrawal

5.27.1.4 When conducting community-based assisted withdrawal programmes, use fixed dose medication regimens[21].

5.27.1.5 Fixed dose or symptom-triggered medication regimens[22] can be used in assisted withdrawal programmes in inpatient or residential settings. If a symptom-triggered regimen is used, all staff should be competent in monitoring symptoms effectively and the unit should have sufficient resources to allow them to do so safely.

[21] A fixed dose regimen involves starting treatment with a standard dose, not defined by the level of alcohol withdrawal, and reducing the dose to zero over 7 to 10 days according to a standard protocol.

[22] A symptom-triggered approach involves tailoring the drug regimen according to the severity of withdrawal and any complications. The service user is monitored on a regular basis and pharmacotherapy is given according to the service user's severity of withdrawal symptoms. Pharmacotherapy only continues as long as the service user is showing withdrawal symptoms.

5.27.1.6 Service users having assisted withdrawal in the community should be regularly medically monitored, at least on alternate days, and a family member or carer should preferably oversee the administration of medication. Adjust the dose if severe withdrawal symptoms or over-sedation occur; use the CIWA-Ar to monitor this.

5.27.1.7 For service users having assisted withdrawal, particularly those who are more severely alcohol dependent or those undergoing a symptom-triggered regimen, consider using a formal measure of withdrawal symptoms such as the CIWA-Ar.

5.27.1.8 Prescribe and administer medication for assisted withdrawal within a standard clinical protocol. The preferred medication for assisted withdrawal in the community is a benzodiazepine (for example, chlordiazepoxide or diazepam). Gradually reduce the dose of the benzodiazepine over 7–10 days to avoid alcohol withdrawal recurring.

5.27.1.9 In a fixed-dose regimen, titrate the initial dose of medication to the severity of alcohol dependence and/or regular daily level of alcohol consumption. In severe alcohol dependence the dosages may need to exceed BNF guidelines to adequately control withdrawal (for example, for service users regularly drinking 60 units of alcohol per day or with an SADQ score of 60, an initial dose of approximately 60 mg chlordiazepoxide four times a day will usually be needed).

5.27.1.10 Be aware that benzodiazepine doses may need to be reduced for children and young people, older people, and people with liver impairment. For people with liver impairment, a short-acting benzodiazepine (for example, lorazepam) may be needed.

5.27.1.11 When managing withdrawal from co-existing benzodiazepine and alcohol dependence increase the dose of benzodiazepine medication used for withdrawal. Calculate the initial daily dose based on the requirements for alcohol withdrawal plus the equivalent regularly used daily dose of benzodiazepine. This is best managed with one benzodiazepine (for example, diazepam or chlordiazepoxide) rather than multiple benzodiazepines. The withdrawal regimen should be extended over 2–3 weeks depending on the severity of co-existing benzodiazepine dependence.

5.27.1.12 When managing alcohol withdrawal in the community, avoid giving people who misuse alcohol large quantities of medication to take home to prevent overdose or diversion. Dispense for up to 2 days at a time.

5.27.1.13 Do not offer clomethiazole for community-based assisted withdrawal because of the risk of overdose and misuse.

5.27.1.14 For managing unplanned acute alcohol withdrawal and complications including delirium tremens and withdrawal-related seizures, refer to NICE clinical guideline 100 on diagnosis and clinical management of alcohol-related physical complications.

5.28 Residential and community settings for the delivery of interventions for alcohol misuse

5.28.1 Introduction

This section assesses the settings that are most clinically and cost effective when it comes to the delivery of interventions to reduce alcohol consumption, promote abstinence and reduce relapse. In the UK most such interventions are provided in community settings usually by a specialist alcohol team. However, some services are provided in residential settings often following a period of residential assisted withdrawal. There is also considerable debate in the UK regarding the value of residential treatment and specifically for which alcohol-related problems a residential unit is most appropriate.

As with the previous reviews, some caution is needed in the assessment and interpretation of the evidence as it is possible that some of the most severely dependent patients may have been excluded from the studies (for example, Pettinati, 1993). In addition as others have identified, it is possible to confuse setting with treatment intensity and duration (for example, Finney, 1996; Mosher *et al.*, 1975). Another problem arises when separating the benefits of a period of inpatient or residential assisted withdrawal from the effects of continued treatment in such a setting (see Walsh *et al.*, 1991). Also, as is the case when evaluating many complex interventions, it is difficult to identify which elements of the intervention are mutative; for example McKay and Rychtarik (2000) evaluated the same treatment in both residential and non-residential settings and reported that the milieu (that is, living in the residential setting for 24 hours a day) added little to the likelihood of a positive outcome of treatment. Relatively few studies in the area report differential outcomes based on patient characteristics, but the picture that does emerge is reasonably consistent. The most commonly studied predictor variables in the treatment of alcohol dependence have been measures of problem severity and social stability. More severe and less socially stable patients who misuse alcohol seem to fare better in inpatient (or more intensive treatment), whereas among married patients with stable accommodation, fewer years of problem drinking, and less history of treatment, outpatient (and less intensive) treatment yields more favourable outcomes than inpatient treatment (Kissin, 1970; McLellan, 1983; Orford, 1976; Smart 1977; Stinson, 1970; Willems, 1973). Finally, some studies provide limited descriptions of the interventions (in particular the comparator interventions) and this, along with the different healthcare systems in which the studies took place, makes interpretation of the evidence challenging.

5.28.2 Clinical review protocol

Information about the databases searched and the inclusion/exclusion criteria used for this section of the guideline can be found in Table 5 (further information about the search for health economic evidence can be found in Chapter 3).

Table 23: Databases searched and inclusion/exclusion criteria for clinical evidence

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Patient population	Diagnosed with having an alcohol use disorder (alcohol dependence or harmful alcohol use)
Interventions	Residential treatment settings versus community treatment settings; duration of residential treatment (long versus short)
Outcomes	Relapse; lapse (non-abstinence); number of participants consuming alcohol; percent days abstinent; drinking frequency measures (for example, mean number of drinking days, number of intoxicated days, number drinking daily); quantity of alcohol measures (for example, drinks per drinking day)

5.28.3 Studies considered[23]

The review team conducted a new systematic search for RCTs and observational studies that assessed the beneficial and detrimental effects of different settings for the delivery of alcohol treatment interventions after an assisted withdrawal programme and related health economic evidence (see Section 1.7.6).

A variety of different treatment settings are described in the research literature. Services were designated as inpatient units; residential units; day hospitals (also known as partial hospitalisation or day centres), or outpatient based interventions of differing intensity and duration (involving attendance at an outpatient clinic, home visits, a combination of both, or containing some limited elements of a day programme). They are in line with the definitions set out in section 1 of this chapter).

It is also important to note that most of the studies included in this review are North American, with few studies conducted in the UK or Europe. They cover a diverse range of populations, including some very specific samples (that is, employment schemes, Veterans Association groups), which may limit generalisation to the UK treatment population.

Fourteen trials met the eligibility criteria set by the GDG, providing data on 2679 participants. All of the studies were published in peer-reviewed journals between 1972 and 2005. Summary study characteristics of the included studies are presented in Table 6. (Further information about both included and excluded studies can be found in Appendix 16c).
A systematic review was only performed for an adult population as there was not enough evidence to perform a meta-analysis for young people and adolescents.

Residential units versus outpatient treatment
Of the 14 included trials, three involved a comparison of residential units versus outpatient treatment. RYCHTARIK2000 compared a residential unit versus an outpatient setting; CHAPMAN1988 compared a 6-week inpatient programme with a 6 week outpatient

[23] Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

programme. WALSH1991 compared compulsory inpatient treatment versus compulsory attendance at Alcoholics Anonymous (AA), this study was atypical in that the sample consisted of workers at an industrial plant in the US who were part of an employee assistance programme, whose jobs were at risk should they fail to attend treatment. A 3-week period of residential treatment was followed by a year of job probation, during which attendance at AA meetings at least three times per week, sobriety at work, and weekly checks with the programme staff were compulsory if the person wanted to keep their job. The outpatient treatment group were referred and offered an escort to a local AA meeting, which they were advised to continue attending at least three times a week for a year. They were treated in the same way as participants in the residential group for the following year.

Residential units versus day hospital

Of the 14 included trials, seven (BELL1994; LONGABAUGH1983; MCKAY1995; MCLACHMAN1982; RYCHTARIK2000; WEITHMANN2005; WITBRODT2007) involved a comparison of residential rehabilitation units versus day hospital. All seven trials had a 28-day length of stay in treatment. Both MCKAY1995 and WITBRODT2007 looked at day hospital versus residential rehabilitation treatment, with the populations being split into a self-selected arm and a randomised arm.

Day hospital versus outpatient treatment

Two trials out of the 14 involved a comparison of day hospital versus outpatient treatment (MORGENSTERN2003; RYCHTARIK2000).

Residential unit versus residential unit

Of the 14 included trials, one (KESO1990) involved a comparison of two different types of residential treatment, assessing the efficacy of two different therapeutic approaches. The Kalliola programme was based on the Hazelden or Minnesota model, with a focus on AA principles with abstinence as the designated treatment goal, whereas the Jarvenpaa programme was a more traditional approach to residential rehabilitation without the focus on AA principles.

Short versus long duration inpatient treatment

Three of the 14 trials involved a comparison of different lengths of admission to inpatient treatment. MOSHER1975 compared a 9-day versus a 30-day inpatient stay. STEIN1975 compared a 9-day residential inpatient stay with a 9-day stay with an additional 25 days of residential rehabilitative care. PITTMAN1972 compared a group receiving 7 to 10 days of inpatient care only with 3 to 6 weeks of inpatient care with an additional option of further outpatient aftercare.

5.28.4 Clinical evidence for residential and community settings for the delivery of alcohol treatment interventions

Evidence from the important outcomes and overall quality of evidence are presented in Table 7, Table 8, Table 9, Table 10 and Table 11. The associated forest plots are in Appendix 17b.

Table 24: Study characteristics table for residential settings

	Residential unit versus outpatient treatment	Residential unit versus day hospital	Day hospital versus outpatient treatment	Residential unit versus residential unit	Short duration versus longer duration inpatient
Total no. of trials (total no. of participants)	3 (N =334)	7 (n= 1453)	1 (n= 382)	1 (n= 141)	3 (n=493)
Study ID	CHAPMAN1988 RYCHTARIK2000 WALSH1991	BELL1994 LONGABAUGH1983 MCKAY1995 MCLACHLAN1982 RYCHTARIK2000 WEITHMANN2005 WITBRODT2007	RYCHTARIK2000 MORGENSTERN2003	KESO1998	MOSHER1975 PITTMAN1975 STEIN1975
Baseline severity: mean (SD)(only for studies that had baseline severity information available)	CHAPMAN1988: Average daily absolute alcohol (g): Inpatient: 256.3 Outpatient: 202.2 Confrontational interview: 226.2 RYCHTARIK2000: DDD (m, SD) Inpatient (n=62) 10.95(8.14) Intensive outpatient (n=69) 10.24(6.62) Standard outpatient (n=61) 10.66(6.77) WALSH1991: Averaged 6.3 drinks a day and 19.8 drinking days in the month preceding interview; 21% had been drink daily and 45%	LONGABAUGH1983 Mean number of days of abstinence in preceding 6 months Inpatient: 7.51 Day:8.28 MCKAY1995: No of days of alcohol intoxication (in previous 30 days): M (SD) Random assignment Day hospital: 16.79(7.29) Inpatient: 12.96(7.64) MCLACHLAN1982 Drunk on average of 295 of previous 365 days Consumed an average of 18 1.5 oz drinks (17 ml) of 40% ethanol per day. RYCHTARIK2000: (refer to first column)	MORGERNSTERN2003 Baseline PDA (m, SD): Inpatient: 48.1 Intensive outpatient: 54.4 Outpatient: 61.8 RYCHTARIK2000 (refer to first column)	Consumption of alcohol 2-month average in grams per day (m, SD) Kalliola AA-type : (Hazelden/ Minnesota model): 112.2(80.3) Jarvenpaa traditional type treatment: 98.3(72.8)	PITTMAN1972 92.3% intoxicated upon admission to treatment, all alcoholism diagnosis

	weekly in previous month	WEITHMANN2005 Drinks per drinking day (30 days prior to admission) (m, SD) Inpatient: 12.3(6.9) Day hospital: 26.6(32.2) % Days abstinent (m, SD) Inpatient: 26.6(32.) Day hospital: 28.6(28.9)			
Treatment length	CHAPMAN1988: 6 weeks RYCHTARIK2000: 28 days WALSH1991: 3 weeks	BELL1994 MCKAY1995 MCLACHLAN1982 RYCHTARIK2000 WEITHMANN2005 Range : 28 days – 31 days LONGABAUGH1983 Range: 2-3 weeks WITBRODT2007: Day hospital: Range 2-3 weeks Residential – up to 60 days	MORGENSTERN2003: Ranged from 22.77 days – 12 weeks RYCHTARIK2000: (see left)	KESO1990: 28 days	MOSHER1975: 9 day versus 21 day PITTMAN1972: 7-20 days versus 3-6 weeks STEIN1975: 9 day versus 21 day
Length of follow-up (if available)	CHAPMAN1988: 6, 18 months RYCHTARIK2000: 6, 9, 12, 15, 18 months WALSH1991: 1, 3, 6, 12, 18, 24 months post-treatment	LONGABAUGH1983: 6,12,18,24 months MCKAY1995: 3, 6, 12 months MCLACHLAN1982: 12 months RYCHTARIK2000: 6, 9, 12, 15, 18 months WEITHMANN2005: 3, 6, 9, 12 months WITBRODT2007:	MORGENSTERN2003: 3,6,9 months	KESO1990: 12 months	MOSHER1975: 3, 6 months PITTMAN1972: 3, 12 months STEIN1975: 2, 4, 7, 10, 13 months

		6, 12 months			
Abstinent or non-abstinent prior to trial		MCKAY1995 Non-abstinent WEITHMAN2005 Combined with initial inpatient assisted withdrawal			
Country	CHAPMAN1988: NEW ZEALAND RYCHTARIK2000 & WALSH1991: US	BELL1994 LONGABAUGH1983 MCKAY1995 RYCHTARIK2000 WITBRODT2007 US MCLACHLAN1982: CANADA WEITHMANN2005: GERMANY	MORGENSTERN2003: US	KESO1990: FINLAND	MOSHER1975 PITTMAN1972 US STEIN1975

Table 25. **Residential unit versus outpatient treatment**

Outcome or subgroup	*k*	Total N	Stats	Effect (95% CI)	Quality of the evidence (GRADE)
1. Abstinence	1	119	SMD mean difference (IV, Random, 95% CI)	Subtotals only	
1.1 Percent days abstinent at 3-month follow-up	1	119	SMD mean difference (IV, Random, 95% CI)	0.22 (-0.14, 0.58)	⊕⊕⊕O MODERATE
2. Drinks per drinking day at 3-month follow-up	1	119	SMD mean difference (IV, Random, 95% CI)	0.02 (-0.34, 0.38)	⊕⊕⊕⊕ HIGH
3. Lapse (number of participants non-abstinent)					
3.1. Lapse at 6-month follow-up	1	46	RR[M-H, Random, 95% CI]	0.92 (0.64,1.32)	⊕⊕⊕O MODERATE
3.2. Lapse at 18 month follow-up	1	48	RR[M-H, Random, 95% CI]	1.30 [0.87, 1.95]	⊕⊕⊕O MODERATE
3.3. Lapse (number of participants non-abstinent)	1	156	RR[M-H, Random, 95% CI]	0.76 (0.61, 0.94)	⊕⊕⊕⊕ HIGH

at 2-year follow-up					
4. Number drinking <60 g absolute alcohol on a drinking day at 6-month follow-up	1	46	RR[M-H, Random, 95% CI]	0.66 (0.26,1.66)	⊕⊕⊕O MODERATE
5. Number drinking <60 g absolute alcohol on a drinking day at 18-month follow-up	1	48	RR[M-H, Random, 95% CI]	0.66 [0.29, 1.48]	⊕⊕⊕O MODERATE

Table 26. Residential unit versus day hospital

Outcome or subgroup	*k*	Total N	Stats	Effect (95% CI)	Quality of the evidence (GRADE)
1. Abstinence					
1.1. Percent days abstinent at 3-month follow-up	1	121	SMD mean difference (IV Random, 95% CI)	0.23 (-0.13,0.59)	⊕⊕⊕O MODERATE
2. Alcohol consumption outcomes	2	169	SMD mean difference (IV Random, 95% CI)	Subtotals only	
2.1. Drinks per drinking day at 3-month follow-up	1	121	SMD mean difference (IV Random, 95% CI)	0.01 (-0.34,0.37)	⊕⊕⊕⊕ HIGH
2.2. Mean number of drinking days at 3-month follow-up	1	48	SMD mean difference (IV Random, 95% CI)	0.33 [-0.24, 0.90]	⊕⊕⊕O MODERATE
2.3. Mean number of drinking days at 6-month follow-up	1	48	SMD mean difference (IV Random, 95% CI)	0.76 (0.17,1.35)	⊕⊕⊕⊕ HIGH
2.4. Mean number of drinking days at 12-month follow-up	1	48	SMD mean difference (IV Random, 95% CI)	0.51 (-0.06,1.09)	⊕⊕⊕O MODERATE
2. Relapse	2	209	RR [M-H, Random, 95% CI]	Total events	
2.1. Post-treatment	1	109	RR [M-H, Random, 95% CI]	0.51 (0.16,1.59)	⊕⊕⊕O MODERATE
2.2. At 12- month follow-up	1	100	RR [M-H, Random, 95% CI]	1.20 (0.69,3.68)	⊕⊕⊕O MODERATE
3. Lapse (non-abstinence)	5	722	RR [M-H, Random, 95% CI]	Subtotals only	

3.1. Number of participants non-abstinent at 6-month follow-up	2	467	RR [M-H, Random, 95% CI]	1.05 (0.82,1.34)	⊕⊕⊕O MODERATE
3.2. Number of participants non-abstinent at 12-monthfollow-up	2	393	RR [M-H, Random, 95% CI]	1.05 (0.88,1.25)	⊕⊕⊕O MODERATE
3.3. Number of participants non-abstinent throughout 12-month follow-up	1	109	RR [M-H, Random, 95% CI]	1.04 (0.86,1.26)	⊕⊕⊕O MODERATE
4. Drinking frequency	3	260	RR [M-H, Random, 95% CI]	Subtotals only	⊕⊕⊕O MODERATE
4.2. Number of participants drinking daily at 6-month follow-up	1	174	RR [M-H, Random, 95% CI]	0.24 (0.03,1.85)	⊕⊕⊕O MODERATE
5. Number not retained in treatment	1	646	RR [M-H, Random, 95% CI]	0.67 (0.52,0.85)	⊕⊕⊕O MODERATE

Table 27: Day hospital versus outpatient treatment

Outcome or subgroup	*k*	Total N	Stats	Effect (95% CI)	Quality of the evidence (GRADE)
1. Abstinence	2	376	SMD mean difference (IV, Random, 95% CI)	Subtotals only	
1.1 Percent days abstinent	2	376	SMD mean difference (IV, Random, 95% CI)	-0.05 [-0.26,0.15]	⊕⊕⊕⊕ HIGH
2. Drinks per drinking day at 3-month follow-up	1	124	SMD mean difference (IV, Random, 95% CI)	0.01 [-0.34,0.36]	⊕⊕⊕⊕ HIGH

Table 28: Residential unit versus residential unit (two different models of treatment)

Outcome or subgroup	*k*	Total N	Stats	Effect (95% CI)	Quality of the evidence (GRADE)
1. Relapse	1	109	RR [M-H, Random, 95% CI]	Subtotals only	
1.1 Number relapsed at 4- to 8-month follow-up	1	109	RR [M-H, Random, 95% CI]	0.79 (0.58,1.08)	⊕⊕⊕O MODERATE
1.2. Number relapsed at 8 to 12-month follow-up	1	109	RR [M-H, Random, 95% CI]	0.87 (0.67,1.13)	⊕⊕⊕O MODERATE

Table 29: Short versus Longer duration inpatient treatment

Outcome or subgroup	*k*	Total N	Stats	Effect (95% CI)	Quality of the evidence (GRADE)
1. Lapse (non-abstinence)	3	513	RR[M-H, Random, 95% CI]	Subtotals only	

1.1 Post-treatment	3	513	RR[M-H, Random, 95% CI]	0.94 (0.84,1.05)	⊕⊕⊕O MODERATE
1.2. At 6-month follow-up	1	200	RR[M-H, Random, 95% CI]	1.05 (0.91,1.21)	⊕⊕⊕O MODERATE
1.3. At 7-month follow-up	1	58	RR[M-H, Random, 95% CI]	0.86 (0.60,1.23)	⊕⊕⊕O MODERATE
1.4. At 10-month follow-up	1	58	RR[M-H, Random, 95% CI]	0.82 (0.58,1.16)	⊕⊕⊕O MODERATE
1.5. At 13-month follow-up	1	58	RR[M-H, Random, 95% CI]	0.95 (0.64,1.40)	⊕⊕⊕O MODERATE
2. Number consuming alcohol 60-90% of the time at 3-month follow-up	1	200	RR[M-H, Random, 95% CI]	0.95 (0.78,1.14)	⊕⊕⊕O MODERATE
3. Number consuming alcohol 60-90% of time at 6-month follow-up	1	200	RR[M-H, Random, 95% CI]	1.09 (0.91,1.30)	⊕⊕⊕O MODERATE
4.Number consuming alcohol less than 60% of time at 3 month follow-up	1	200	RR[M-H, Random, 95% CI]	1.01[0.82,1.24]	⊕⊕⊕O MODERATE
3. Number consuming alcohol less than 60% of time at 6-month follow-up	1	200	RR[M-H, Random, 95% CI]	0.82[0.61,1.09]	⊕⊕⊕O MODERATE

5.28.5 Clinical evidence summary

Residential unit versus outpatient treatment

Residential unit treatment was no more effective than an outpatient setting in maintaining abstinence or in reducing the number of drinks per drinking day at 3-month follow-up (RYCHTARIK2000). Furthermore, there was no significant difference observed between treatment in a residential unit and a day hospital in reducing the number of participants drinking more than 60g of alcohol per drinking day at 6-month follow-up (CHAPMAN1988).

A residential unit setting was significantly more effective than an outpatient setting in increasing the number of participants abstinent at 2-year follow-up in only one study (WALSH 1991). This study population was atypical and is unlikely to be representative of patients attending UK alcohol treatment services, and the study included treatment elements that would be difficult to replicate in the UK.

Based on the GRADE method outlined in Chapter 3, the quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (for further information, see Table 7).

Residential unit versus day hospital

On measures of alcohol consumption, there was no significant difference between a residential unit and a day hospital on drinks per drinking day at 3-month follow-up. At 6-month follow-up, there was a significant difference between the two groups favouring day hospital treatment on mean number of drinking days, based on the results of the MCKAY1995 study. This effect did not remain at 12-month follow-up, however there was a trend (p=0.08) slightly favouring day hospital treatment. It should be noted that this study had both a randomised and self-selected sample, and since inclusion into this analysis was restricted to RCTs, only the randomised population was used. However, the results from the self-selected sample parallel the results from the randomised arm. The self-selected participants did not do any better on drinking outcomes than those who were randomly assigned at 6- or 12-month follow-up. Any differences that did emerge from the self-selected group, tended to favour the partial hospitalisation group (day hospital), as found in the randomised sample.

On rates of relapse or lapse to alcohol at 6 and 12 months post-treatment, there were no significant differences between residential unit and day hospital treatment. Additionally, there were no significant differences in the number of participants drinking daily at 6-month follow-up (LONGABAUGH1983), or in the percentage of days abstinent at 3-month follow-up (RYCHTARIK2000).

One study found that more participants were retained in treatment in the residential setting than the day hospital setting (BELL1994). However, this study included a mixture of participants with primary drug and alcohol problems, and so the results may not be representative of individuals presenting to an alcohol treatment service.

Based on the GRADE methodology outlined in Chapter 3, the quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (for further information see Table 8).

Day hospital versus outpatient treatment

A day hospital was not found to be any more effective than a less intensive outpatient setting in terms of percentage days abstinent or drinks per drinking day at 3-month follow-up. However, it is important to consider that the MORGENSTERN2003 study contained a mixture of both primary drug and alcohol users, so these results may not be generalisable to the wider population presenting for treatment of alcohol problems.

Based on the GRADE methodology outlined in Chapter 3, the quality of this evidence is *moderate* to *high* and further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (for further information, see Table 9).

Residential unit versus residential unit

When analysing two different therapeutic approaches to residential treatment, no difference was found between the two different residential treatment models (Kalliolla and Jarvenpaa) on reducing the number of participants who relapsed from 4- through 12-month follow-up.

Based on the GRADE methodology outlined in Chapter 3, the quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (for further information, see Table 10).

Short duration versus longer duration level (inpatient)

There was no significant difference between a 21-day inpatient stay and an extended 9-day inpatient stay at reducing the number of participants consuming alcohol post-treatment, or at 3- or 6-month follow-up (MOSHER1975). A longer duration in an inpatient setting was no more effective in preventing lapse (non-abstinence) than a shorter duration in an inpatient setting. No effect remained at 6-, 7-, 10- and 13-month follow-up.

Based on the GRADE methodology outlined in Chapter 3, the quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (for further information, see Table 11).

5.28.6 Additional trials assessing different treatment settings

RCTs

There are several additional studies that were well-conducted trials but did not meet guideline criteria for inclusion in the initial analysis which was based on a comparative review of the different treatment settings identified above. These studies nevertheless found similar results that support this meta-analysis. Chick

(1988) compared simple advice with amplified advice (simple advice plus one session of motivational interviewing) with extended treatment, which included the offer of further outpatient appointments, inpatient, or day treatment. There were no differences between the advice groups or the extended treatment on abstinence outcomes at 2- year follow-up, nor on drinking frequency outcomes. There were no significant differences found on alcohol consumed in 7 days prior to follow-up, frequency of drinking over 200g per day in the past year, period of abstinence in the past year, or on other measures such as employment or marital situation. Edwards and Guthrie (1967) assigned participants to an average of 9 weeks of inpatient or outpatient treatment, and found no significant differences on measures of drinking at 6- and 12-month follow-up. Lastly, Eriksen (1986) assigned 17 alcoholics post-assisted withdrawal to either immediate inpatient treatment or a 4-week waiting list control. Results indicated no significant differences between groups on outcomes of days drinking, or on other outcomes such as sick leave or institutionalisation.

Observational studies

Due to the nature of alcohol misuse and the problems of consenting severely dependent participants, it is not always possible to conduct RCTs that compare treatment modalities. Consequently, there are a number of important observational studies that add value to the RCT data presented above. For the purpose of this guideline, and in order to obtain an overview of the available literature, observational studies that have met other methodological criteria are described in the evidence summaries of the individual treatment programmes. In one non-randomised study participants chose their own length of admission that is either a short stay of 7 days or a longer additional stay of 8 to 21 days (Foster *et al.,* 2000), and in two naturalistic studies, shorter inpatient stays were compared with existing, longer programmes (Long *et al.,* 1998; Trent, 1998); no significant differences were found between the different durations of treatment.

Predictor studies

Even in the absence of overall differences in treatment outcomes between residential and outpatient settings, it is possible that certain types of patients derive differential benefits or harms from being treated in these alternative settings. This is the central issue in matching patients to optimal treatment approaches. Relatively few of the above studies report differential outcome based on patient characteristics but a reasonably consistent picture does emerge, although it should be pointed out this is often based on post hoc analysis of non-randomised populations and so should be treated with caution. The GDG consider this issue, the main evidence points which are summarised below; in doing so the GDG drew on the existing systematic review developed by the Specialist Clinical Addiction Network (SCAN, 2006) for the consensus statement on in-patient treatment.

The most commonly studied predictor variables in the treatment of alcohol dependence have been measures of problem severity and social stability. More severe and less socially stable patients who misuse alcohol seem to fare better in inpatient or more intensive treatment (possibly outpatient based) , whereas among married patients with stable accommodation, fewer years of problem drinking, and less history of treatment, outpatient (and less intensive) treatment yields more favourable outcomes than inpatient treatment (Kissin, 1970; McLellan, 1983; Orford, 1976; Smart, 1977; Stinson, 1970; Willems, 1973). When heterogeneous populations of

alcoholics are averaged together, the consistent finding is of comparable (or better) outcomes from outpatient as opposed to residential treatment (McLellan 1983). Moos and colleagues (1999) found in an effectiveness trial of inpatient treatment of different theoretical orientations within the Veterans Association treatment system that longer lengths of stay were associated with better outcomes. Likewise, in Project MATCH, patients who received inpatient treatment prior to 12 weeks of outpatient care had better drinking outcomes than those who went directly into OP care (Project MATCH Research Group, 1997).

5.28.7 Health economic evidence

Systematic literature review

No evidence on the cost effectiveness of different settings for rehabilitation treatment for people with an alcohol use disorder (alcohol dependence or harmful alcohol use) was identified by the systematic search of the economic literature. Details on the methods used for the systematic search of the economic literature are described in Chapter 3.

Cost analysis of rehabilitation treatment in different settings

The cost effectiveness of rehabilitation treatment for people with an alcohol use disorder in different settings was considered by the GDG as an area with potentially significant resource implications. A formal economic evaluation comparing different rehabilitation settings was not attempted due to time constraints and problems in synthesising relevant clinical evidence. Nevertheless, a cost analysis was undertaken to estimate costs associated with rehabilitation treatment of people with alcohol use disorders in different settings in the UK. The results of this analysis were considered by the GDG alongside the findings of the clinical effectiveness review, in order to make a judgement regarding the cost effectiveness of different settings for rehabilitation treatment.

Two different settings for rehabilitation treatment were considered in the analysis: residential settings and day hospital (partial hospitalisation) settings. The healthcare resource use estimates for each setting were based on descriptions of resource use in studies included in the systematic literature review of clinical evidence. Studies conducted in the UK were limited in this review. Therefore, resource use estimates from studies conducted outside the UK were refined using the expert opinion of the GDG in order to reflect current routine clinical practice within the NHS. The estimated resource use was subsequently combined with national unit costs in order to provide a total cost associated with rehabilitation treatment in the three settings assessed. Unit costs were derived from national sources (Curtis, 2009; DH, 2010) and reflected 2009 prices.

Residential treatment unit

The duration of treatment in this setting has been reported to vary from 4 weeks (Sannibale *et al.*, 2003) to 60 days (Zemore *et al.*, 2008). Both studies were conducted outside the UK. The GDG estimated that residential treatment lasts 12 weeks (3 months) in the UK setting. No unit costs for residential treatment for people with an alcohol use disorder provided within the NHS are available. Residential units for people who misuse drugs/alcohol provided by the voluntary sector cost £808 per resident week (Curtis, 2009). By combining estimated duration of residential

treatment with the respective unit cost, the total cost of residential rehabilitation treatment is estimated at £9,696.

Day hospital treatment

According to Zemore and colleagues (2008) and McKay and colleagues (1995), the duration of rehabilitation treatment taking place in day hospitals ranges between 2 and 4 weeks. The GDG considered 4 weeks to be a reasonable duration of day hospital rehabilitation in the UK. McKay and colleagues (1995) reported that participants in their study attended a day hospital 5 days per week. The GDG estimated that frequency of attendance in day hospital rehabilitation should be between 5 and 7 days per week. UK unit costs of such services are not available. The NHS unit cost of mental health day care is £102 per attendance (DH, 2010). However, this facility is likely to provide, on average, non-specialist services and therefore this unit cost is expected to be somewhat lower than the cost of a day hospital rehabilitation service. On the other hand, Parrott and colleagues (2006) reported a local unit cost of a day hospital assisted withdrawal and rehabilitation service for people with alcohol dependence of £129 per day (uplifted from the originally reported cost of £109 per day in 2004 prices, using the Hospital and Community Health Services pay and prices inflation indices provided in Curtis [2009]). Using the range of these two unit costs, and combining them with the estimated resource use, the total cost of a day hospital rehabilitation treatment for people with alcohol use disorders is estimated to range from £2,040 (for a 5-day per week programme, using the lower unit cost) to £3,612 (for a 7-day per week programme, using the higher unit cost).

Summary

The cost analysis indicates that, as expected, day hospital treatment is less costly than residential rehabilitation.

5.28.8 Clinical and health economic evidence summary

A range of treatment settings were reviewed for treatment taking place after an assisted withdrawal programme. These included: inpatient facilities, residential units, outpatient treatment, and day hospital treatment. For all the treatment settings, the evidence in support of them was assessed to be of a high or moderate quality using GRADE profiles.

Overall, inpatient settings were not seen as any more effective than outpatient, or day hospital settings. The exception to this was that day hospital settings were favoured over inpatient settings in one study on improving drinking outcomes at 6- and 12-month follow-up. Additional time in an inpatient setting did not improve outcomes, and a standard, shorter, inpatient stay seemed to be equally as effective.

Furthermore, three studies (BELL 1994, MORGENSTERN 2003, WITBRODT 2007) included patients with both drug and alcohol problems and it can be difficult to disentangle the effects on those with a primary alcohol problem. However, alcohol data were reported separately from other substances and it was possible to use these data in this review.

The studies also include a wide range of different programmes. For example, the nature of the outpatient programmes in these studies varied considerably in content,

duration and intensity. However, he results of the meta-analysis are in line with the findings of previous reviews assessing the effectiveness of residential versus non residential treatment (e.g. Finney, 1996). A cost analysis undertaken for this guideline indicated that day hospital treatment incurs considerably lower costs than residential treatment.

Taking both cost and clinical effectiveness evidence into account, these results suggest that once an assisted withdrawal programme has been completed; a psychosocial treatment package delivered in a non-residential day hospital or community treatment programme[24] is likely to be the more cost-effective option.

5.28.9 From evidence to recommendations

The evidence from this review suggests that community settings are at least as effective as residential units and less costly in providing effective treatment for harmful alcohol misuse and alcohol dependence and therefore are recommended as the preferred setting for delivering effective treatment. For some of the more severely dependant patients there is some evidence to suggest that more intensive programme are more effective, but the GDG took the view that these intensive programme can also be provided in the community in the form of day hospital or similarly intensive community-based programmes. The GDG took the view that a small number of people with alcohol dependence may benefit from residential treatment after an assisted withdrawal; in identifying this sub-group homelessness was identified by the GDG as the most important factor.

5.28.10 Recommendations

5.28.11 Interventions to promote abstinence and relapse prevention

5.28.11.1 For people who are alcohol dependent and homeless, consider offering residential rehabilitation for a maximum of 3 months. Help the service user find stable accommodation before discharge.

5.28.12 Research Recommendations

5.28.12.1 For people who are moderately and severely dependent on alcohol and have significant comorbid problems, is an intensive residential rehabilitation programme clinically and cost effective when compared with intensive community-based care?

This question should be answered using a prospective cohort study of all people who are moderately and severely dependent on alcohol entering residential and intensive community rehabilitation programmes in a purposive sample of alcohol treatment services in the UK. It should report short- and medium-term outcomes (including cost-effectiveness outcomes) of at least 18 months' duration. Particular attention should be paid to the characterisation of the treatment environment and the nature of the interventions provided in order to inform the analysis of moderators and

[24] Note the cost of such a programme are likely to be lower than a day hospital programme given its reduced intensity

mediators of treatment effect. The outcomes chosen should reflect both observer and service user-rated assessments of improvement (including personal and social functioning) and the acceptability of the intervention. The study needs to be large enough to determine the presence or absence of clinically important effects, and mediators and moderators of response should be investigated. A cohort study has been chosen as the most appropriate design as previous studies in this area that have attempted to randomise participants to residential or community care have been unable to recruit clinically representative populations.

Why this is important?

Many people, in particular those with severe problems and complex comorbidities, do not benefit from treatment and/or lose contact with services. One common approach is to offer intensive residential rehabilitation and current policy favours the provision of such care. However, the research on the effectiveness of residential rehabilitation is uncertain with a suggestion that intensive community services may be as effective. The interpretation of this research is limited by the fact that many of the more severely ill people are not entered into the clinical trials because some clinicians are unsure of the safety of the community setting. However, clinical opinion is divided on the benefits of residential rehabilitation, with some suggesting that those who benefit are a motivated and self-selected group who may do just as well with intensive community treatment, which is currently limited in availability. Given the costs associated with residential treatment and the uncertainty about outcomes, the results of this study will have important implications for the cost effectiveness and provision of alcohol services in the NHS.

6. Psychological and psychosocial interventions in the treatment and management of alcohol misuse

6.1 Introduction

This Chapter is concerned with structured psychological interventions used to help people who experience alcohol dependence or harmful alcohol use. These approaches have been the focus of much research and debate over the years.

Psychological interventions for people experiencing harmful alcohol use or dependence have traditionally made use of the interaction between a person with an alcohol problem and a therapist, worker, helper or counsellor (the latter terminologies may vary depending on services and settings). In addition, more recently, there has been some growth and expansion in the use of self help based interventions that involve the use of DVDs, books, computer programmes or self-help manuals.

Psychological approaches vary depending on the theoretical models underpinning them. Broadly, psychological interventions can be classified into behavioural, cognitive, psychodynamic, humanistic, motivational, disease, and social and environmental. The emphasis of each therapy is different, depending on the theoretical underpinning of the approach. Behavioural approaches for example are based on the premise that excessive drinking is a learned habit and therefore influenced by principles of behaviour. The latter can hence be used to teach the individual a different behavioural pattern that will reduce the harm emerging from excessive drinking. Cognitive approaches on the other hand, emphasise the role of thinking and cognition either prior to engaging in drinking behaviour or in order to prevent or avoid lapse or relapse. Social approaches focus the work on the social environment, e.g. families or wider social networks. In some instances, a combination of approaches is used and described under the term of 'multimodal' treatment, guided by the rationale that a combination of approaches is more powerful than each individual component. Each category of intervention is discussed in more detail later in this Chapter within sub-Sections describing the studies reviewed that are relevant to each type of approach.

Whilst the rationale and theoretical frameworks for treatments have been clearly articulated in the various research studies, the evidence for the superiority of one form of treatment over another in the field of alcohol has been difficult to find (Miller & Wilbourne, 2002). This has led to the general view in the field that whilst psychological interventions are better than no intervention, no one approach is superior to another. In this chapter where available the evidence for each psychological intervention is assessed in relation to 3 comparators: (i) is the intervention superior to treatment as usual or a control condition? (ii) is the intervention superior to other interventions? and (iii) is the intervention superior to

other variants of the same type of approach (e.g. behavioural cue exposure vs. behavioural self-control training)?

The review of this literature is of significant importance, given the potential wide use of psychological interventions in NHS and non-statutory services and the need to provide an evidence base to inform and guide the implementation and use of these approaches. It is important to note that previous influential reviews of alcohol treatment (e.g. 'Mesa Grande' Miller & Wilbourne, 2002) have combined findings from a large number of trials that included a wide range of populations (e.g. opportunistic versus help-seeking; mild versus severe dependence). In the current review, only studies that involved treatment seeking populations experiencing harmful drinking or alcohol dependence were included and therefore the number of trials meeting these criteria was reduced in order to make them relevant to the population addressed in this guideline.

Finally, psychological treatments can also be used to help people experiencing harmful alcohol use or dependence in order to address coexisting problems such as anxiety and depression. Psychological treatments can also be used to help people who misuse alcohol address coexisting disorders such as anxiety and depression. These approaches are not covered within this review and the reader is referred to the separate NICE guidelines that address psychological interventions for specific mental health problems. Healthcare professionals should note that, although the presence of alcohol misuse may impact, for example, on the duration of a formal psychological treatment, there is no evidence supporting the view that psychological treatments for common mental disorders are ineffective for people with alcohol misuse. A number of NICE mental health guidelines have specifically considered the interaction between common mental health problems and drug and alcohol use. For example, NICE guidelines such as for anxiety (NICE, 2004) or obsessive-compulsive disorder (NICE, 2006) provide advice on assessment and the impact that drug and alcohol misuse may have on the effectiveness or duration of treatment. There is also some evidence to suggest that the active treatment of comorbid mental health problems may improve drug and alcohol substance misuse outcomes (Charney *et al.,* 2001; Hesse, 2004; Watkins *et al.,* 2006). This may be particularly important for service users who have achieved abstinence (note that symptoms of depression and anxiety may remit following successful treatment of the alcohol problem), but whose alcohol use is at risk of returning or escalating due to inadequately treated anxiety or depression.

6.1.1 Current practice

Services for people with alcohol dependence and harmful alcohol use are commonly delivered by statutory and non-statutory providers. The field is undergoing rapid change across different areas of the country due to the impact of the commissioning process. Traditionally services have been provided by teams where the detoxification and counselling aspects of treatment have been fairly clearly separated. Within the NHS, teams tend to consist of different disciplines including nurses, counsellors, medical practitioners and less often other professions such as psychologists and occupational therapists. Teams are commonly under-resourced with practitioners having high caseloads and limited access to supervision. Most practice involves an eclectic approach that combines strategies from various psychological approaches. A more recent development involves contracts between commissioners and providers

that may determine for example the number of sessions to be delivered yet this is rarely informed by the evidence and tends to be driven by pragmatic or resource issues (Drummond *et al,* 2005).

Whilst the research literature to date, has concentrated mostly on the comparison of well defined treatment interventions commonly incorporated into treatment manuals, this stands in contrast to what is normally delivered in routine practice. Despite the research on psychological treatments, current UK practice is not underpinned by a strong evidence base and there is wide variation in the uptake and implementation of psychological approaches to treatment across services (Drummond *et al,* 2005).

A number of factors may contribute to the low implementation of evidence based psychological interventions. First, there is a lack of availability of reviews of the current evidence in a clear and practical format that can be accessible to practitioners, managers and commissioners. This has led to a weak dissemination of the evidence base concerning psychological interventions for alcohol problems within routine service provision. Second the varied composition of the workforce with a range of training experiences, not all of which include training in the delivery of psychological interventions. Furthermore as noted by Tober *et al*., (2005) training programmes for the management of substance misuse vary widely in content with no consensus on methods to provide and evaluate such training or to maintain its effects. Supervision of psychological interventions is equally varied and not always available. Finally, there is a tendency in the field to eclecticism fuelled by the perception that all approaches are either equally valid or equally ineffective.

6.2 Therapist factors

Several therapist factors that could potentially affect treatment have been considered, including demographics, professional background, training, use of supervision and competence. Two related aspects are dealt with below, namely the therapeutic alliance and therapist competence.

6.2.1 The therapeutic alliance

There are various definitions of the therapeutic alliance, but in general terms it is viewed as a constructive relationship between therapist and client, characterised by a positive and mutually respectful stance in which both parties work on the joint enterprise of change. Bordin (1979) conceptualised the alliance as having three elements comprising the relationship between therapist and patient: agreement on the relevance of the tasks (or techniques) employed in therapy, agreement about the goals or outcomes the therapy aims to achieve, and the quality of the bond between therapist and patient.

There has been considerable debate about the importance of the alliance as a factor in promoting change, with some commentators arguing that technique is inappropriately privileged over the alliance, a position reflected in many humanistic models where the therapeutic relationship itself is seen as integral to the change process, with technique relegated to a secondary role (for example, Rogers, 1951). The failure of some comparative trials to demonstrate differences in outcome between active psychological therapies (for example, Elkin, 1994; Miller & Wilbourne, 2002) is often cited in support of this argument and is usually referred to

as 'the dodo-bird hypothesis' (Luborsky *et al*., 1975). However, apart from the fact that dodo-bird findings may not be as ubiquitous as is sometimes claimed this does not logically imply that therapy technique is irrelevant to outcome. Identifying and interpreting equivalence of benefit across therapies remains a live debate (for example, Ahn & Wampold, 2001; Stiles *et al*., 2006) but should also include a consideration of cost effectiveness as well as clinical efficacy (NICE, 2008a).

Meta-analytic reviews report consistent evidence of a positive association of the alliance with better outcomes with a correlation of around 0.25 (for example, Horvath & Symonds, 1991; Martin *et al*., 2000), a finding that applies across a heterogeneous group of trials (in terms of variables such as type of therapy, nature of the disorder, client presentation, type of measures applied and the stage of therapy at which measures are applied). However, it is the consistency, rather than the size of this correlation, which is most striking, since a correlation of 0.25 would suggest it could account for only 6% of the variance in the outcome. Specific studies of the role of the alliance in drug and alcohol treatment programmes have been conducted. Luborsky and colleagues (1985), Connors and colleagues (1997) and Ilgen and colleagues, (2006) reported a relationship between treatment outcomes but others (e.g. Ojehagen *et al;* 1997) have not. Ojehagen and colleagues suggest that this discrepancy between the various studies may have arisen from methodological differences between the studies; in contrast to Luborsky *et al* and Connors *et al* and Ilgen *et al,* in Ojehagen *et al,* ratings of the alliance were made by an independent rater from video tapes as opposed to rating made by the therapist early in treatment. This is consistent with other studies; for example Feeley and colleagues (1999) reported that alliance quality was related to early symptom change. Therefore, it seems reasonable to debate the extent to which a good alliance is necessary for a positive outcome of an intervention, but it is unlikely to be sufficient to account for the majority of the variance in outcome.

6.2.2 Therapist competence

Studies of the relationship between therapist competence and outcome suggest that all therapists have variable outcomes, although some therapists produce consistently better outcomes (for example, Okiishi *et al*., 2003). There is evidence that more competent therapists produce better outcomes (Barber *et al*., 1996, 2006; Kuyken & Tsivrikos, 2009). This is also the case for psychological interventions in the alcohol field, the Project MATCH Research Group (1998) report therapist differences which impact on outcome. A number of studies have also sought to examine more precisely therapist competence and its relation to outcomes; that is, what is it that therapists do in order to achieve good outcomes? A number of studies are briefly reviewed here.

This section, draws on a more extensive review of the area by Roth and Pilling (2010) which focused on CBT as this area had the most extensive research. In an early study, Shaw and colleagues (1999) examined competence in the treatment of 36 patients treated by eight therapists offering CBT as part of the National Institute of Mental Health trial of depression (Elkin *et al*., 1989). Ratings of competence were made on the Cognitive Therapy Scale (CTS). Although the simple correlation of the CTS with outcome suggested that it contributed little to outcome variance, regression analyses indicated a more specific set of associations; specifically, when controlling for pre-therapy depression scores, adherence and the alliance, the overall CTS score

accounted for 15% of the variance in outcome. However, a subset of items on the CTS accounted for most of this association.

Some understanding of what may account for this association emerges from three studies by DeRubeis's research group (Feeley *et al*., 1999; Brotman *et al*., 2009). All of the studies made use of the Collaborative Study Psychotherapy Rating Scale (CSPRS: Hollon *et al*., 1988), subscales of which contained items specific to CBT. On the basis of factor analysis, the CBT items were separated into two subscales labelled 'cognitive therapy – concrete' and 'cognitive therapy – abstract'. Concrete techniques can be thought of as pragmatic aspects of therapy (such as establishing the session agenda, setting homework tasks or helping clients identify and modify negative automatic thoughts). Both DeRubeis and Feeley (1990) and Feeley and colleagues (1999) found some evidence for a significant association between the use of 'concrete' CBT techniques and better outcomes. The benefits of high levels of competence over and above levels required for basic practice has been studied in most detail in the literature on CBT for depression. In general, high severity and comorbidity, especially with Axis II pathology, have been associated with poorer outcomes in therapies, but the detrimental impact of these factors is lessened for highly competent therapists. DeRubeis and colleagues (2005) found that the most competent therapists had good outcomes even for patients with the most severe levels of depression. Kuyken and Tsivrikos (2009) found that therapists who are more competent have better patient outcomes regardless of the degree of patient comorbidity. In patients with neurotic disorders (Kingdon *et al*., 1996) and personality disorders (Davidson *et al*., 2004), higher levels of competence were associated with greater improvements in depressive symptoms. Although competence in psychological therapies is hard to measure in routine practice, degrees of formal training (Brosan *et al.,* 2007) and experience in that modality (James *et al*., 2001) are associated with competence and are independently associated with better outcomes (Burns & Nolen-Hoeksema, 1992). All therapists should have levels of training and experience adequate to ensure a basic level of competence in the therapy they are practicing, and the highest possible levels of training and experience are desirable for those therapists treating patients with severe, enduring or complex presentations. In routine practice in services providing psychological therapies for depression, therapists should receive regular supervision and monitoring of outcomes. Roth et al, (2010) reviewed the training programmes associated with clinical trials as part of a programme exploring therapist competence (Roth and Pilling, 2008). They showed that clinical trials are associated with high levels of training, supervision and monitoring; factors which are not always found in routine practice. This is part due the inadequate description of training programmes in the trial reports. However, there is an increasing emphasis on describing the process of training in clinical trials, the report by Tober *et al.* (2005) being a notable recent publication describing the training programme for the UK Alcohol Treatment Trial.

Trepka and colleagues (2004) examined the impact of competence by analysing outcomes in Cahill and colleagues' (2003) study. Six clinical psychologists (with between 1 and 6 years post-qualification experience) treated 30 clients with depression using CBT, with ratings of competence made on the CTS. In a completer sample (N=21) better outcomes were associated with overall competence on the CTS (r= 0.47); in the full sample this association was only found with the 'specific CBT skills' subscale of the CTS. Using a stringent measure of recovery (a BDI score no

more than one SD from the non-distressed mean), nine of the 10 completer patients treated by the more competent therapists recovered, compared with four of the 11 clients treated by the less competent therapists. These results remained even when analysis controlled for levels of the therapeutic alliance.

Miller et al (1993) looked at the relationship of therapist behaviour in a brief (2 session) "motivational check-up"; they identified one therapist behaviour (a confrontational approach) which was associated with increased alcohol intake. Agreeing and monitoring homework is one of the set of 'concrete' CBT skills identified above. All forms of CBT place an emphasis on the role of homework because it provides a powerful opportunity for clients to test their expectations. A small number of studies have explored whether compliance with homework is related to better outcomes, although rather fewer have examined the therapist behaviours associated with better client 'compliance' with homework itself. Kazantzis and colleagues (2000) report a meta-analysis of 27 trials of cognitive and/or behavioural interventions that contained data relevant to the link between homework assignment, compliance and outcome. In 19 trials clients were being treated for depression or anxiety; the remainder were seen for a range of other problems. Of these, 11 reported on the effects of assigning homework in therapy and 16 on the impact of compliance. The type of homework varied, as did the way in which compliance was monitored, although this was usually by therapist report. Overall there was a significant, although modest, association between outcome and assigning homework tasks ($r = 0.36$), and between outcome and homework compliance ($r = 0.22$). While Kazantzis and colleagues (2000) indicate that homework has greater impact for clients with depression than anxiety disorders, the number of trials on which this comparison is made is small and any conclusions must therefore be tentative.

Bryant and colleagues (1999) examined factors leading to homework compliance in 26 clients with depression receiving CBT from four therapists. As in other studies, greater compliance with homework was associated with better outcome. In terms of therapist behaviours, it was not so much therapists' CBT-specific skills (such as skilfully assigning homework or providing a rationale for homework) that were associated with compliance, but ratings of their general therapeutic skills, and particularly whether they explicitly reviewed the homework assigned in the previous session. There was also some evidence that compliance was increased if therapists checked how the client felt about the task being set and identified potential difficulties in carrying it out.

6.3 Matching effects/severity

One of the main challenges in providing services for alcohol treatment is to increase the effectiveness of the interventions offered. The concept of tailoring treatments to particular types of clients in order to increase effectiveness has been appealing to researchers both in terms of its logical plausibility and as a possible explanation for the reason that no one intervention has universal effectiveness. However, despite this, there is limited evidence to date that matching alcohol misusing or alcohol dependent clients to treatment approaches demonstrates effectiveness.

In 1989 the National Institute on Alcohol Abuse and Alcoholism (NIAAA) began the largest national multisite RCT of alcoholism treatment matching entitled Matching

Alcoholism Treatments to Client Heterogeneity (Project MATCH). This study outlined matching hypotheses which were investigated across both 'outpatient' and 'aftercare' settings following inpatient or day hospital treatment. Clients were randomly allocated to one of three manual guided treatment approaches individually offered, namely, Cognitive Behavioural Coping Skills Therapy, Motivational Enhancement Therapy or Twelve Step Facilitation Therapy (Project MATCH Research Group, 1997). However, tests of the primary matching hypotheses over the 4 to 15 month follow up period revealed few matching effects. Of the variables considered, psychiatric severity was considered an attribute worthy of further consideration as this alone appeared to influence drinking at one year follow up. A UK trial later explored client treatment matching in the treatment of alcohol problems comparing MET with Social Behaviour Network Therapy (UKATT Research Team, 2007), the findings of which strongly supported those of Project MATCH in that none of the five matching hypotheses was supported at either follow up point on any outcome measure.

Despite the limited findings from these major trials, other studies have detected more positive conclusions which have highlighted methodological considerations associated with matching. Several studies have acknowledged the usefulness of matching treatment approaches for individuals who are experiencing severe psychiatric co-morbidity. In a trial comparing alcohol dependent clients with a range of psychiatric impairments, more structured coping skills training yielded lower relapse rates at 6-month follow-up (Kadden *et al*, 1989). Studies which looked specifically at matching in the context of psychiatric disturbance have acknowledged that the severity of the psychiatric presentation has a negative impact upon the relapse rates (Brown *et al*, 2002) although matching appears to have assisted in retaining individuals in treatment (McLellan *et al*, 1997). Although in some cases no significant differences have been detected between overall relapse rates when matching treatments at 2 years follow-up, relapse to alcohol was found to have occurred more slowly where high psychiatric co-morbidity is matched with more structured coping skills training (Cooney *et al*, 1991).

The importance of service user choice in relation to self-matching treatments has been associated with more positive outcomes in two studies (Brown *et al*, 2002: UKATT, 2007), whilst other trials have emphasized the negative consequences of 'mismatching' including earlier relapse (Cooney *et al*, 1991), poorer outcomes (Karno & Longabaugh, 2007) and increased need of support services (Conrod *et al*, 2000).

Treatment providers are now required to consider not only treatment efficacy but cost effectiveness and for this reason, treatment matching has remained an appealing option (Moyer *et al*, 2000). However, for the findings of matching trials to be meaningful, one must consider a variety of methodological issues. Many of the recent studies considered have involved small samples, comparing a diverse range of variables both in terms of sample characteristics and treatment process factors (McLellan & Alterman, 1991). It has been suggested that for trials to provide more meaningful findings, there is a need for a clearer focus on matching questions which then focus upon well-specified treatments that have clear goals with specific patient populations. In this way, such designs may be more likely to provide interpretable results as well as a clearer understanding of the processes likely to be responsible for such findings.

Despite the steady development of patient-treatment matching studies in relation to alcohol dependence, the outcomes to date indicate that there is no one single treatment that is effective for all clients. There continue to be many obstacles to matching clients to specific treatment programmes in real world settings and for many organisations patient-treatment matching remains impractical. Research would appear to indicate that the nature and severity of co-morbid and complex presentations such as, psychiatric disturbance do have a negative impact upon treatments for addiction and this is arguably an area for further research (McLellan *et al*, 1997). It has been suggested that given the diversity of presentations and the large number of variables implicated in such research, the development of reliable and generalisable measures will be important for both the effective training and evaluation of treatment-matching efficacy (McLellan & Alterman, 1991).

6.4 Setting the context for TSF and AA

The twelve step principles were first set out in a publication by Alcoholics Anonymous (AA) in the 1950s. AA describes itself as a 'Fellowship' and AA groups are widely available in the UK as support networks for the people with alcohol dependence. AA is a self-help movement with the 12-step principles at the core. The 12 steps lay out a process that individuals are recommended to follow, based on an assumption that dependence on alcohol is a disease and therefore a goal of lifelong abstinence should be promoted. Membership is entirely voluntary and free of charge, there is a spiritual element to participation and life-long membership is encouraged. Attendance has been associated with successful abstinence from alcohol in a number of studies (see Ferri *et al*., 2006 for a systematic review).

Most 12 step treatment is predicated on the understanding that the treatment would fail without subsequent attendance at 12 step fellowship meetings. However, a common problem in the treatment of alcohol dependence with AA or 12-step groups is that alcohol misusers frequently discontinue AA involvement at the end of their designated treatment period and usually do not continue with aftercare treatment (Kaskutas *et al*., 2002; Kelly *et al*., 2003; Moos *et al*., 2001; Tonigan *et al*., 2003). As a result, manual guided Twelve-Step Facilitation (TSF) has been developed as an active stand-alone or adjunctive intervention which involves: introducing the alcohol misuser to the principles of AA and the 12 steps of treatment (e.g. Project MATCH Research Group, 1993), providing information on AA facilitates in the geographical area, and engaging with the client in setting goals for attendance and participation in the meetings. The aim of TSF is to maintain abstinence whilst in treatment and to sustain gains made after treatment concludes. This guideline is concerned with the use of TSF as an active intervention in the treatment of alcohol dependence and harmful alcohol use. An evaluation of the classic AA approach is outside the scope of this guideline.

6.5 Review of psychological therapies

6.5.1 Aim of review

This section aims to review the evidence for psychological interventions without pharmacological interventions for the treatment of alcohol dependence and harmful

alcohol use. The literature reviewed in this Section is focused on a reduction or cessation of drinking and hence assesses any outcomes pertaining to this. Most of the literature in the field is focused on adults over the age of 18 years. However, for young people under the age of 18 years old, literature assessing the clinical efficacy of psychological therapies for alcohol misuse alone (without comorbid drug abuse) is limited. The psychological evidence below is for an adult population only and a review of the evidence for the treatment of young people is described in Section **Error! Reference source not found.**.

Psychological interventions were considered for inclusion in the review if they were:-

- Planned treatment
- For treatment-seeking participants only (of particular importance for the brief interventions as our scope did not cover opportunistic brief interventions – see scope Appendix 1)
- Manual-based or in the absence of a formal manual, the intervention should be well-defined and structured
- Ethical and safe

The following psychological therapies used in the treatment of alcohol misuse were considered for inclusion in this guideline:-

- Brief Interventions (Planned only)
    - e.g. psychoeducational and motivational techniques
- Self-Help Based Treatments
    - Brief Self-Help Interventions (including guided self help/bibliotherapy)
- Twelve-Step Facilitation
- Cognitive Behavioural Based Therapies
    - Standard Cognitive Behaviour Therapy (CBT)
    - Coping Skills
    - Social Skills Training
    - Relapse Prevention
- Behavioural Therapies
    - Cue Exposure
    - Behavioural Self-Control Training
    - Contingency Management
    - Aversion Therapy
- Motivational Enhancement Therapy
- Social Network and Environment Based Therapies
    - Social Behaviour and Network Therapy
    - The Community Reinforcement Approach
- Counselling
    - Couples Therapy (including including behavioural couples therapy and other variants of couples therapy)
- Family-based Interventions
    - Functional Family Therapy
    - Brief Strategic Family Therapy
    - Multi-systematic Therapy
    - 5 Step Family Interventions
    - Multi Dimensional Family Therapy
    - Community Reinforcement and Family Training

- Psychodynamic Therapy
  - Short-term Psychodynamic Intervention
  - Supportive Expressive Psychotherapy

In addition, physical therapies such as meditation and acupuncture are also covered in this review.

Good quality RCT evidence for the clinical efficacy of some of the psychological therapies listed was not always available. Therefore, the evidence summaries in this chapter describe the psychological therapies for which evidence of sufficient quality (see methods Chapter 3 for methodological criteria) was available. There are a number of useful studies which add value to the RCT data presented and they are included in this review. For the purpose of this guideline, and in order to obtain an overview of the available literature, studies that have met other methodological criteria are described in the evidence summaries of the individual therapies.

Full characteristics of included studies, forest plots and GRADE profiles can be found in Appendix 16d, 17c & 18c respectively as there were too extensive to place within this chapter.

6.5.2 Clinical questions

Primary clinical questions addressed in this chapter

1. For people with alcohol dependence or harmful alcohol use is psychological *treatment x* when compared to *y* more clinically and cost-effective and does this depend on:
   - Presence of comorbidities
   - Subtypes (matching effects)
   - Therapist-related factors (quality, therapeutic alliance, competence, training, etc.)

6.6 Outcomes

There were no consistent critical outcomes across studies and outcomes were mainly continuous in nature. This variability in outcomes poses some difficulties in pooling data from different studies. Therefore, continuous outcomes were grouped into three categories:-

- Abstinence e.g.
  - Percentage/Proportion days abstinent
  - Abstinent days per week/month
  - Longest duration abstinent
- Rates of Consumption e.g.
  - Percentage/Proportion days heavy drinking
  - Drinking days per month
  - Days drinking greater than X drinks per week
- Amount of Alcohol Consumed e.g.
  - Drinks per drinking day
  - Mean number of drinks per week
  - Grams of alcohol per drinking day
  - Number of drinks per drinking episode

Dichotomous outcomes included:

- Abstinence (number of participants abstinent)
- Lapse (number of participants who have drank at all)
- Relapse (number of participants who have drank more than X number of drinks)
- Attrition (the number of participants leaving the study for any reason)

Studies varied in their definition of these dichotomous terms. For example, the number of drinks defined as constituting a relapse varied.

6.7 Motivational Techniques

6.7.1 Definition

Motivational Enhancement Therapy (MET) is the most structured and intensive motivational-based intervention. It is based on the methods and principles of motivational interviewing (Miller *et al*., 1992). It is patient-centred and aims to result in rapid internally motive changes by exploring and resolving ambivalence towards behaviour. The treatment strategy of motivational interviewing is not to guide the client through recovery step by step, but to use motivational methods and strategies to utilise the patient's resources. A more specific manualised and structured form of motivational interviewing based on the work of Project MATCH is usually utilised (Project Match Research Group, 1993).

Brief motivational interventions include the computerised Drinker's Check Up which assesses symptoms of dependence, alcohol related problems and motivation for change, and 'feedback, responsibility, advice, menu, empathy, self-efficacy' (FRAMES; Bien *et al*., 1993).

6.7.2 Clinical review protocol (Motivational Techniques)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21 of this Chapter).

Table 30. Clinical review protocol for the review of Motivational Techniques.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Motivational Techniques
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.7.3 Studies considered for review [25]

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of motivational techniques in the treatment of alcohol dependence or harmful alcohol use. See Table 2 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Eight trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on 4209 participants. All eight studies were published in peer-reviewed journals between 1997 and 2007. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was not meeting drinking quantity/diagnostic criteria, i.e. participants were not drinking enough to be categorised as harmful or dependent drinkers or less than 80% of the sample meet criteria for alcohol dependence or harmful alcohol use. Other reasons were that treatment was opportunistic as opposed to planned, the study was not directly relevant to the clinical questions, or no relevant alcohol-focused outcomes were available. A list of excluded studies can be found in Appendix 16d.

Motivational techniques versus minimal intervention control

Of the eight included trials, three involved a comparison of motivational techniques versus control met criteria for inclusion. HESTER2005 assessed the drinker's check-up versus waiting list control; ROSENBLUM2005b investigated MET plus relapse

[25] Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

prevention versus information and referral only; and SELLMAN2001 assessed MET versus feedback only. The included studies were conducted between 2001 and 2005. The five year follow-up outcomes were obtained from Adamson & Sellman (2008).

Motivational techniques versus *other active intervention*

Of the eight included trials, six assessed MET versus another active intervention met criteria for inclusion. DAVIDSON2007 investigated MET versus cognitive behavioural broad spectrum therapy; MATCH1997 assessed MET versus both CBT and TSF; SELLMAN2001 compared MET with non-directive reflective listening (counselling); SHAKESHAFT2002 assessed FRAMES with CBT; SOBELL2002 compared motivational enhancement/personalized feedback with psychoeducational bibliotherapy/drinking guidelines; and lastly UKATT2005 investigated MET versus social behaviour and network therapy (SBNT). The included studies were conducted between 1997 and 2007.

Table 31. Summary of study characteristics for motivational techniques

	Motivational vs. Minimal Intervention Control	Motivational vs. Other Active Intervention
***K*(total N)**	3(433)	6(3818)
Study ID	HESTER2005 ROSENBLUM2005b SELLMAN2001	DAVIDSON2007 MATCH1997 SELLMAN2001 SHAKESHAFT2002 SOBELL2002 UKATT2005
Diagnosis (when reported)	DSM alcohol dependent/abuse ROSENBLUM2005b DSM alcohol dependent SELLMAN2001 AUDIT score of 8+ HESTER2005	DSM alcohol dependent DAVIDSON2007 SELLMAN2001 DSM alcohol dependent /abuse MATCH1997 UKATT2005
Baseline severity	HESTER2005 *Drinks per drinking day: approx 7* SELLMAN2001 *Mild/moderate dependence* *Unequivocal heavy drinking 6+ times (in six months prior to treatment): 90.2%*	DAVIDSON2007 *-Percent days abstinence: approx 30%* *-Percent days heavy drinking: approx 63%* MATCH1997 *-Percent days abstinent: approx 30%* *-Drinks per drinking day: approx 16 drinks* SELLMAN2001 *-Unequivocal heavy drinking 6+ times in six months prior to treatment: 90.2%* SHAKESHAFT2002 *-Weekly Australian units per week: approx 32 units* SOBELL2002 *-Number of drinking days per week: approx 5.5 days* *-Drinks per drinking day: approx 5* UKATT2005 *-Percent days abstinent: 29.5%* *-Number of drinks per drinking day: 26.8 drinks*
Number of sessions	Range: 1-12 sessions	Range: 1-12 sessions
Length of treatment	Range: 1 – 6 weeks	Range: 1-12 weeks
Length of Follow-up	Range: 1 month – 5 years	Range: 6 months – 5 years
Setting	Outpatient Treatment Centre SELLMAN2001 Computer Based Intervention HESTER2005 Homeless Soup Kitchen ROSENBLUM2005b	Outpatient Treatment Centre DAVIDSON2007 SELLMAN2001 SHAKESHAFT2002 UKATT2005 Clinical Research Unit MATCH1997 Mail Information SOBELL2002
Treatment Goal	Drinking Reduction/Moderation ROSENBLUM2005b Abstinence OR Drinking Reduction/Moderation HESTER2005 Not explicitly stated SELLMAN2001	Abstinence OR Drinking Reduction/Moderation DAVIDSON2007 MATCH1997 UKATT2005 Not explicitly stated SELLMAN2001 SHAKESHAFT2002 SOBELL2002
Country	HESTER2005 (USA) ROSENBLUM2005b (USA) SELLMAN2001 (New Zealand)	DAVIDSON2007 (USA) MATCH1997 (USA) SELLMAN2001 (New Zealand) SHAKESHAFT2002 (Australia) SOBELL2002 (USA) UKATT2005 (UK)

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6.7.4 Evidence summary[26]

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Motivational techniques versus minimal intervention control

One computerized session of MET (drinker's check up) was significantly better than control in reducing average drinks per day at 1 month follow up (moderate effect size). However, this finding as based on the results of a single study. Furthermore, no significant difference in average drinks per day and drinks per drinking day was observed between the drinker's check up and control at two and twelve month follow-up.

MET (with relapse prevention) (ROSENBLUM2005b) was significantly more effective than control at reducing heavy alcohol use when assessed at 5 month follow up (moderate effect size). This was further supported by the SELLMAN2001 study which favoured MET over control in the number of people who drank excessively and frequently (10 or more drinks, 6 or more times) at 6 month follow up (large effect size). However, this effect was not observed at long follow-up assessment (5 years). Although no significant difference was observed between groups in reducing the days ANY alcohol was drank, the analyses showed a trend favouring MET with relapse prevention over control (p=0.07). No significant difference in attrition rates were observed between MET and control groups across studies.

The quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 3.

Motivational techniques versus other active intervention

The clinical evidence showed that no significant difference could be found between motivational techniques and other active interventions in maintaining abstinence at up to 15 month follow-up. Furthermore, no difference between groups was observed in reducing the number of participants who had lapsed or reducing heavy drinking at all follow-up points.

Other therapies (namely CBT and TSF) were more effective than motivational techniques in reducing the quantity of alcohol consumed when assessed post treatment. However, the effect size was small (0.1) and was no longer seen at longer follow up points of 3 to 15 months.

No significant difference was observed between groups in attrition rates post treatment or at 3 month follow up. However, other therapies were more effective at retaining participants at 6 month follow-up (low effect size). Follow-up periods longer than 6 months did not indicate any significant difference between groups.

[26] Sensitivity analyses were conducted to assess the effect of combining studies investigating brief motivational techniques with structured MET studies. The findings were found to be robust in sensitivity analysis and the effects found were not determined by the intensity and duration the motivational intervention.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 4.

Table 32. Motivational Techniques vs. Control Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Es
Lapse or Relapse			
Lapsed up until 6 month follow-up			
at 6 months	82	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.7
Lapsed >12 month follow-up			
at 5 yr follow-up	56	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.7
Amount of Alcohol Consumed			
Amount of Alcohol Consumed up to 6 month follow up			
Average Drinks Per Day (log transformed) over entire assessment period at 1 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.67 [-1.2
Average Drinks Per Day (log transformed) over entire assessment period at 2 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.46 [-0.9
Drinks per drinking day (log transformed) at 1 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.6
Drinks per drinking day (log transformed) at 2 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.3
Amount of Alcohol consumed 7-12 month follow up			
Average Drinks Per Day (log transformed) over entire assessment period at 12 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.7
Drinks per drinking day (log transformed) at 12 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	0.36 [-0.1
Rates of Consumption			
Rates of Consumption up to 6 month follow up			
Days any alcohol use at 5 month follow up	139	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-0.6
Days Heavy alcohol use (>4 drinks) at 5 month follow up	46	Std. Mean Difference (IV, Random, 95% CI)	-0.70 [-1.3
Rate of consumption up to 6 month follow-up			
Exceeded national drinking guidelines at least once at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.66
Exceeded national drinking guidelines 6 or more times at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.66
Drank 10+ standard drinks at least once at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.58
Drank 10+ or more drinks 6 or more times at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.43
Rates of Consumption >12 month follow-up			
Exceeded national drinking guidelines at least once at 5 year follow-up	56	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.60
Exceeded national drinking guidelines 6 or more times at 5 year follow-up	56	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.52
Drank 10+ standard drinks at least once at 5 year follow-up	56	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.34
Drank 10+ or more drinks 6 or more times at 5 year follow-up	56	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.29
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	290	Risk Ratio (M-H, Random, 95% CI)	1.09 [0.76
Attrition (drop-out) up to 6 months follow-up	82	Risk Ratio (M-H, Random, 95% CI)	Not esti
at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	Not esti
Attrition (drop-out) at 7-12 month follow-up	61		
at 12 months	61	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.30
Attrition (drop-out) > 12 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.68
at 5 year follow-up	82	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.68

Table 33. Motivational Techniques vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinent Post Treatment	1801	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.02, 0.18]
Abstinence up to 6 months follow-up	2476	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.06, 0.10]
at 3 month follow-up	835	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.12, 0.30]
at 6 month follow-up	1641	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.11, 0.10]
Abstinence - 7-12 months follow-up			
at 9 month follow-up	1616	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.06, 0.15]
at 12 month follow-up	1672	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.07, 0.15]
Abstinence > 12 month follow-up			
at 15 month follow-up	1573	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.05, 0.16]
Lapse or Relapse			
Lapsed up to 6 month follow-up			
at 6 months	82	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.78, 1.10]
Lapsed >12 month follow-up			
at 5 yr follow-up	48	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.75, 1.40]
Rates of Consumption			
Rate of consumption Post Treatment			
% heavy drinking days	149	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.27, 0.37]
Rate of consumption up to 6 month follow-up	115	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.35, 0.38]
Binge consumption (occasions in prior 30 days where at least 7 (males) or 5 (females) drinks consumed at 6 months	115	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.35, 0.38]
Rate of consumption up to 6 month follow-up			
Exceeded national drinking guidelines at least once at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.63, 1.10]
Exceeded national drinking guidelines 6 or more times at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.63, 1.10]
Drank 10+ standard drinks at least once at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.60, 1.07]
Drank 10+ or more drinks 6 or more times at 6 month follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.45, 1.05]
Rate of consumption - 7-12 month follow-up			
Number of days drinking per week at 12 month follow up	657	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.15, 0.15]
Days > 5 drinks at 12 months	657	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.23, 0.08]
Rates of Consumption >12 month follow-up			
Exceeded national drinking guidelines at least once at 5 year follow-up	48	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.61, 1.51]
Exceeded national drinking guidelines 6 or more times at 5 year follow-up	48	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.47, 1.53]
Drank 10+ standard drinks at least once at 5 year follow-up	48	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.41, 1.88]
Drank 10+ or more drinks 6 or more times at 5 year follow-up	48	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.38, 3.61]

Table 4. Motivational Techniques vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Amount of Alcohol Consumed			
Amount of alcohol consumed post treatment			
Drinks per Drinking Day	1652	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.00, 0.20]
Amount of alcohol consumed up to 6 month follow-up	2380	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.04, 0.13]
Drinks per drinking day at 3 month follow-up	624	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.20, 0.12]
Drinks per drinking day at 6 month follow-up	1641	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.02, 0.18]
Drinks per week at 6 months	115	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.27, 0.46]
Amount of alcohol consumed 7-12 month follow-up			
Drinks per Drinking Day at 9 month follow-up			
Drinks per Drinking Day at 12 month follow-up	2771	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.07, 0.08]
Drinks per week at 12 months	657	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.16, 0.14]
Amount of alcohol consumed >12 month follow up			
Drinks per Drinking Day at 15 month follow-up	1573	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.05, 0.16]
Attrition (Drop-Out)			
Attrition (drop-out) post treatment	2022	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.31, 1.59]
Attrition (drop-out) up to 6 months follow-up	2719	Risk Ratio (M-H, Random, 95% CI)	1.37 [1.05, 1.80]
at 3-month follow-up	762	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.84, 2.18]
at 6 month follow-up	1957	Risk Ratio (M-H, Random, 95% CI)	1.38 [1.00, 1.92]
Attrition (drop-out) at 7-12 months follow-up			
at 9 month follow-up	1641	Risk Ratio (M-H, Random, 95% CI)	1.85 [0.83, 4.11]
at 12-month follow-up	3130	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.87, 1.52]
Attrition (drop-out) > 12 month follow-up	1676	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.55, 1.35]
at 15 month follow-up	1594	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.52, 3.08]
at 5 year follow-up	82	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.45, 1.27]

6.8 Twelve-Step Facilitation (TSF)

6.8.1 Definition

Twelve-Step Facilitation (TSF) is based on the twelve-step or Alcoholics Anonymous (AA) concept that alcoholism is a spiritual and medical disease (see Section 6.4 for a discussion of AA). As well as a goal of abstinence, this intervention aims to actively encourage commitment to and participation in AA meeting. Participants are asked to keep a journal of AA attendance and participation and are given AA literature relevant to the 'step' of the programme the client patient has reached. TSF is highly structured and manualised (Nowinski *et al*., 1992) and involves a weekly session in which the patient is asked about their drinking, AA attendance and participation, given an explanation of the themes of the current sessions, and goals for AA attendance are set.

6.8.2 Clinical review protocol (Twelve-Step Facilitation)

Information about the databases searched and the inclusion/exclusion criteria used for this section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 34. Clinical review protocol for the review of twelve-step facilitation (TSF)

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	TSF
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.8.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of TSF in the treatment of alcohol dependence or harmful alcohol use. See Table 6 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Six trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=2556 participants. All six studies were published in peer-reviewed journals between 1997 and 2009. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was the studies were assessing the efficacy of twelve-step groups (i.e. AA) directly (not twelve-step facilitation) and hence were also naturalistic studies. Other reasons included a drug and not alcohol focus, secondary analysis and not being directly relevant to the current guideline. A list of excluded studies can be found in Appendix 16d.

TSF versus other active intervention

Of the six included trials, five compared TSF with another active intervention. The comparator against TSF was CBT (EASTON2007), couples therapy and psychoeducational intervention (FALSSTEWART2005; FALSSTWEART2006), MET and CBT (MATCH1997), and coping skills (WALITZER2009).

Comparing different formats of TSF

Two included studies assessed one form of TSF versus another. TIMKO2008 evaluated intensive TSF versus standard TSF. In the standard TSF condition, alcohol misusers were given an AA schedule and encouraged to attend sessions. Counsellors and patients reviewed relapse prevention, but treatment was more focused on

psychoeducation. In the intensive TSF condition, standard treatment was provided and counsellors actively arranged AA meeting attendance. Participants were encouraged to keep an AA attendance journal. WALITZER2009 assessed a directive approach to TSF versus a motivational approach to TSF in addition to treatment-as-usual (coping skills).

Table 35. Summary of study characteristics for Twelve-Step Facilitation (TSF)

	TSF vs. Other Active Intervention	Different formats of TSF
***K*(total N)**	5(1221)	2(456)
Study ID	EASTON2007 FALSSTEWART2005 FALSSTWEART2006 MATCH1997 WALITZER2009	TIMKO2008 WALITZER2009
Diagnosis (when reported)	DSM alcohol dependent EASTON2007 FALSSTEWART2005 DSM IV alcohol dependent/abuse FALSSTWEART2006 MATCH1997	
Baseline severity	EASTON2007 *-Approx 19 years of alcohol use* *-Alcohol use in past 28 days: approx 6 days* FALSSTEWART2005 *-Percent day heavy drinking: 56-59% across treatment groups* FALSSTEWART2006 *-Percent days abstinent: 40-44% across treatment groups* MATCH1997 *-Percent days abstinent: approx 30%* *-Drinks per drinking day: approx. 16 drinks* WALITZER2009 *-Percent days abstinent: 35.4%* *-Percent days heavy drinking: 32.7%*	TIMKO2008 *-ASI alcohol score: approx 0.28* WALITZER2009 *-Percent days abstinent: 35.4%* *-Percent days heavy drinking: 32.7%*
Number of sessions	Range: 12-32 sessions	1 session (TIMKO2007) and 12 sessions (WALITZER2009) in which TSF was in addition to other treatment
Length of treatment	12 weeks	Unclear
Length of Follow-up	Range: 3-15 months	Range: 3-12 months
Setting	Outpatient Treatment Centre EASTON2007 FALSSTEWART2005 FALSSTWEART2006 WALITZER2009 Clinical Research Unit MATCH1997	Outpatient Treatment Centre TIMKO2008 WALITZER2009
Treatment Goal	Abstinence FALSSTWEART2006 Drinking Reduction/Moderation EASTON2007 Abstinence OR Drinking Reduction/moderation MATCH1997 Not explicitly Stated FALSSTEWART2005 WALITZER2009	Not explicitly stated TIMKO2008 WALITZER2009
Country	All USA	All USA

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6.8.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

TSF versus ***other active intervention***

The clinical evidence revealed no significant difference between TSF and other active interventions in maintaining abstinence, reducing heavy drinking episodes when assessed post-treatment and various at follow-up points up to 12 months. TSF was significantly better than other active intervention in reducing the amount of alcohol consumed when assessed at 6 month follow-up. However, the effect size was small (SMD=-0.09) and no significant difference between groups was observed for any other follow-up points.

No significant difference in attrition rates were observed between TSF and other active interventions in attrition post-treatment and up to 6 month follow up. However, those receiving TSF were more likely to be retained at 9 month follow-up, although his difference was not observed at 12 and 15 month follow-up.

The quality of this evidence is *high* therefore further research is unlikely to change our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 7.

Comparing different formats of TSF

Directive TSF was more effective at maintaining abstinence than motivational TSF up to 12 month follow-up (RR = -0.41 to -0.81 across follow-up points). However, no difference between groups was observed in reducing heavy drinking episodes.

In addition, intensive TSF was significantly more effective than standard TSF in maintaining abstinence at 12 month follow-up (RR = 0.81).

No significant difference between TSF methods was observed in attrition post-treatment or at various follow-up points up to 12 months.

Additionally, KAHLER2004 was identified as assessing brief advice to facilitate AA involvement versus a motivational enhancement approach to facilitate AA involvement. This study could not be included in analyses as data could not be extracted. However, the study reported that although AA attendance was associated with better drinking outcomes, the more intensive motivational enhancement format of facilitating involvement did not involvement in AA and hence did not result in better alcohol outcomes.

The quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (see Appendix 18c). An evidence summary of the results of the meta-analyses can be seen in Table 8.

Table 36. Twelve-Step Facilitation vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimat
Abstinence			

Abstinence Post Treatment	1860	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.10, 0.18
Abstinence up to 6 month follow-up			
% days abstinent at 3 month follow-up	340	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.41, 0.31
% days abstinent at 6 month follow-up	1975	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.23, 0.16
Abstinence 7-12 month follow-up			
% days abstinent at 9 month follow-up	1942	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.18, 0.18
% days abstinent at 12 month follow-up	1911	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.21, 0.19
Abstinence > 12 month follow-up			
at 15 month follow-up	1573	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.12, 0.09
Rates of Consumption			
Rate of alcohol consumption Post Treatment			
% days heavy drinking at post-treatment	99	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.47, 0.45
Rate of alcohol consumption up to 6 month follow-up			
% days heavy drinking at 3 month follow-up	301	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.43, 0.17
% days heavy drinking at 6 month follow-up	296	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.42, 0.26
Rate of alcohol consumption - 7-12 month follow-up			
% days heavy drinking at 9 month follow-up	288	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.14, 0.40
% days heavy drinking at 12 month follow-up	282	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.28, 0.58
Amount of Alcohol Consumed			
Amount of alcohol consumed Post Treatment	1651	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.13, 0.15
Amount of alcohol consumed up to 6 month follow-up			
at 6 month follow-up	2194	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.17, -0.0
Amount of alcohol consumed 7-12 month follow-up			
at 9 month follow up	1615	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.15, 0.06
at 12 month follow up	1594	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.20, 0.01
at 6 month follow-up	1640	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.19, 0.01
Amount of alcohol consumed > 12 month follow-up			
at 15 month follow up	1573	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.14, 0.02
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	1864	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.73, 1.70
Attrition (Drop-Out) up to 6 month follow up			
at 3 month follow-up	227	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.19, 1.73
at 6 month follow-up	1853	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.29, 5.11
Attrition (Drop-Out) 7-12 months follow-up			
at 9 month follow-up	1837	Risk Ratio (M-H, Random, 95% CI)	0.37 [0.15, 0.88
at 12 month follow-up	1930	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.55, 2.65
Attrition (Drop-Out) > 12 month follow-up			
at 15 month follow-up	1594	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.16, 1.37

Table 37. Comparing Different Formats of Twelve-Step Facilitation Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
% Days Abstinent up to 6 months follow up			
at 3 month follow-up	102	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.79, -0.0
at 6 month follow-up	97	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.81, -0.0
% Days Abstinent 7-12 months follow up			
at 9 month follow-up	95	Std. Mean Difference (IV, Random, 95% CI)	-0.57 [-0.98, -0.1
at 12 month follow-up	95	Std. Mean Difference (IV, Random, 95% CI)	-0.58 [-0.99, -0.1
Lapse or Relapse			
Number of participants Lapsed 7-12 months follow-up			
at 12 month follow-up	307	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.66, 1.00
Rates of Consumption			
% Days Heavy Drinking up to 6 month follow up			
at 3 month follow-up	102	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.59, 0.19

at 6 month follow-up	97	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.47, 0.33
% Days Heavy Drinking at 7-12 month follow up			
at 9 month follow-up	95	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.60, 0.20
at 12 month follow-up	95	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.50, 0.31
Attrition (Drop-Out)			
Attrition (Drop-out) Post Treatment	345	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.55, 1.84
Attrition (Drop-out) up to 6 month follow up			
at 3 month follow-up	111	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.06, 1.44
at 6 month follow-up	102	Odds Ratio (M-H, Fixed, 95% CI)	1.53 [0.24, 9.57
Attrition (Drop-out) 7-12 months follow-up			
at 9 month follow-up	97	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.07, 15.86
at 12 month follow-up	440	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.52, 2.06

6.9 Cognitive Behavioural Therapy

6.9.1 Definition

Cognitive behavioural therapy encompasses a range of therapies in part derived from the cognitive behavioural model of affective disorders, in which the patient works collaboratively with a therapist using a shared formulation to achieve specific treatment goals. Such goals may include recognising the impact of behavioural and/or thinking patterns on feeling states and encouraging alternative cognitive and/or behavioural coping skills to reduce the severity of target symptoms and problems. Cognitive behavioural therapies include standard cognitive behavioural therapy (CBT), relapse prevention, coping skills and social skills training.

Standard Cognitive Behavioural Therapy (CBT)

Standard CBT is a discrete, time-limited, structured psychological intervention, derived from a cognitive model of drug misuse (Beck *et al*., 1993). There is an emphasis on identifying and modifying irrational thoughts, managing negative mood and intervening after a lapse to prevent a full-blown relapse.

Relapse-prevention

A CBT adaptation based on the work of Marlatt, this incorporates a range of cognitive and behavioural therapeutic techniques to identify high risk situations, alter expectancies and increase self-efficacy. This differs from standard CBT in the emphasis on training people who misuse alcohol to develop skills to identify situations or states where they are most vulnerable to alcohol use, to avoid high-risk situations, and to use a range of cognitive and behavioural strategies to cope effectively with these situations (Annis, 1986; Marlatt & Gordon, 1985).

Coping and Social Skills Training

Coping and social skills training is a variety of cognitive behavioural therapy that is based on social learning theory of addiction and the relationship between drinking behaviour and life problems (Marlatt & Gordon, 1985; Kadden *et al*., 1992). Treatment is manual-based (Marlatt & Gordon, 1985) and involves increasing the individual's ability to cope with high-risk social situations and inter-personal difficulties.

6.9.2 Clinical review protocol (Cognitive Behavioural Therapies)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 38. Clinical review protocol for the review of Cognitive Behavioural Therapies.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Cognitive Behavioural Therapies
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

6.9.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of cognitive behavioural therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 10 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Twenty RCT trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=3970 participants. All twenty studies were published in peer-reviewed journals between 1986 and 2009. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). When studies did meet basic methodological inclusion criteria, the main reasons for exclusion were not having alcohol-focused outcomes that could be used for analysis, and not meeting drinking quantity/diagnosis criteria, i.e. participants were not drinking enough to be categorised as harmful or dependent drinkers or less than 80% of the sample meet criteria for alcohol dependence or harmful alcohol use. Other reasons were that the study was outside the scope of this guideline, presented secondary analyses, and was drugs focused or did not differentiate between drugs and alcohol and were focused on aftercare. A list of excluded studies can be found in Appendix 16d.

Cognitive Behavioural Therapies versus treatment-as-usual or control[27]

Three studies compared cognitive behavioural therapy versus TAU or control. BURTSCHEIDT2002 assessed CBT versus coping skills versus TAU (unstructured, non-specific support and therapy). MONTI1993 investigated cue exposure with coping skills against control (un-specified TAU and daily cravings monitoring). ROSENBLUM2005b assessed relapse prevention with MET versus control (information and referral only).

Cognitive Behavioural Therapies versus other active intervention

Thirteen studies assessed CBT versus another active intervention. CONNORS2001 was complex in design and investigated alcohol-focused coping skills, with/without the addition of life coping skills, with/without the addition of psychoeducational intervention at different intensities. Additionally, the study investigated the difference between low and high intensity treatment of these conditions. The results of the thirty month follow-up were obtained from Walitzer & Connors (2007). The other studies included in this analyses were DAVIDSON2007 (broad-spectrum treatment versus MET); EASTON2007 (CBT versus TSF); ERIKSEN1986 and LITT2003 (both assessed coping skills versus group counselling); LAM2009 (coping skills versus BCT with/without parental skills training); MATCH1997 (CBT versus both MET and TSF); MORGENSTERN2007 (coping skills with MET versus M*ET* alone); SANDAHL1998 (relapse prevention versus psychodynamic therapy); SHAKESHAFT2002 (CBT versus FRAMES); SITHARTHAN1997 (CBT vs. cue exposure); VEDEL2008 (CBT versus BCT); and WALITZER2009 (coping skills versus TSF).

Comparing different formats of cognitive behavioural therapy

Six studies investigated one form of cognitive behavioural therapy versus another form of cognitive behavioural therapy. BURTSCHEIDT2002 investigated CBT versus coping skills; MARQUES2001 assessed group versus individual cognitive behavioural psychotherapy; CONNORS investigated different intensities of alcohol-focused coping skills; LITT2009 assessed a packaged CBT program versus an individual assessment treatment program which was cognitive behavioural in nature; MONTI1990 investigated communication skills training (both with and without family therapy) as well as cognitive behavioural mood management training. ROSENBLUM2005a investigated relapse prevention versus relapse prevention with motivational enhancements.

[27] Treatment-as-usual (TAU) and control were analysed together because TAU was un-structured, un-specified and brief and similar to what would be classified as control in other studies.

Table 39. Summary of study characteristics for Cognitive Behavioural Therapies

	Cognitive Behavioural Therapies vs. TAU or Control	Cognitive Behavioural Therapies vs. Other Active Intervention	Different formats of Cognitive Behavioural Therapy
***K*(total N)**	3(450)	13(2956)	6(771)
Study ID	BURTSCHEIDT2002 MONTI1993 ROSENBLUM2005b	CONNORS2001 DAVIDSON2007 EASTON2007 ERIKSEN1986 LAM2009 LITT2003 MATCH1997 MORGENSTERN2007 SANDAHL1998 SHAKESHAFT2002 SITHARTHAN1997 VEDEL2008 WALITZER2009	BURTSCHEIDT2002 MARQUES2001 CONNORS LITT2009 MONTI1990 ROSENBLUM2005a
Diagnosis (when reported)	DSM alcohol dependent BURTSCHEIDT2002 MONTI1993	DSM alcohol dependent CONNORS2001 DAVIDSON2007 EASTON2007 SANDAHL1998 DSM dependent/abuse LAM2009 LITT2003 MATCH1997 MORGENSTERN2007 VEDEL2008	DSM /ICD alcohol dependent BURTSCHEIDT2002 MARQUES2001 CONNORS2001 MONTI1990 DSM alcohol dependent/abuse LITT2009 ROSENBLUM2005a

	Cognitive Behavioural Therapies vs. TAU or Control	Cognitive Behavioural Therapies vs. Other Active Intervention	Different formats of Cognitive Behavioural Therapy

Baseline severity	MONTI1993 *-ADS score: 20.7* *-SMAST score: 9.97* *-Drinks per drinking day: 12.1 drinks* *-Percent days abstinent: 47%* *-Percent days heavy drinking: 45%*	CONNORS2001 *-Percent of sample severe dependence: 8.3%* *-Percent of sample moderate dependence: 66%* *-Percent of sample mild dependence: 18.1%* DAVIDSON2007 *-Percent days abstinence: approx 30%* *-Percent days heavy drinking: approx 63%* EASTON2007 *-Approx 19 years of alcohol use* *-Alcohol use in past 28 days: approx 6 days* ERIKSEN1986 *-Previous alcoholism inpatient status: 66.7%* LAM2009 *Percent days abstinent: approx 37%* LITT2003 *-Drinking days 6 months prior to intake: 72%* MATCH1997 *-Percent days abstinent: approx 30%* *-Drinks per drinking day: approx. 16 drinks* MORGENSTERN2007 *-Drinks per drinking day: 9.5 drinks* *-ADS core: 12.2* SANDAHL1998 *-Duration of alcohol abuse: 11 years* *-Reported morning drinking:75.5%* SHAKESHAFT2002 *-Weekly Australian units per week: approx 32 units* SITHARTHAN1997 *-SADQ-C score: 18.81* *-ICQ score: 13.05* *-CDSES score: 35.93* *-Drinking days/ month: 20.2 days* *-Consumption/ occasion: 8.82 drinks* VEDEL2008 *-62% alcohol dependent* *-50% when drinking drank 7+ units* *-57% drank daily or nearly daily* WALITZER2009 *-Percent days abstinent: 35.4%* *-Percent days heavy drinking: 32.7%*	MARQUES2001 *-Number of drinking days-in last 90 days: 49 days* *-Number of heavy drinking days in last 90 days : 34.5 days* *-Number of problem drinking days in last 90 days: 16.5 days* *-Mean weekly consumption: 36.5 drinks* *-SADD score abstinence/ moderate rates: 17* CONNORS2001 *-Percent of sample severe dependence: 8.3%* *-Percent of sample moderate dependence: 66%* *-Percent of sample mild dependence: 18.1%* *-Average monthly abstinent days: 10.1 days* *-Average monthly light days: 6.1 days* *-Average monthly moderate days: 8 days* *-Average monthly heavy days: 5.7 days* LITT2009 *-Proportion days abstinence: 0.19 days* *-Proportion days heavy drinking: approx 0.59 days* MONTI1990 *-Percent possible drinking days abstinent: approx 43%* *-Number of drinks per possible drinking day: 11 drinks* *-No. of drinks per actual drinking day: 17 drinks* *-Percent possible drinking days in which heavy drinking: 45%* ROSENBLUM2005a *-Days abstinent in past 30 days: 14 days* *-ASI alcohol score: approx 0.47*
	Cognitive Behavioural Therapies vs. TAU or Control	**Cognitive Behavioural Therapies vs. Other Active Intervention**	**Different formats of Cognitive Behavioural Therapy**

Number of sessions	Range: 6-26 sessions	Range: 6-26 sessions	Range: 12-23 sessions
Length of treatment	Range: 2 weeks – 6 months	Range: 10 weeks – 6 months	Range: 6-10 weeks
Length of Follow-up	Range: 0-6 months	Range: 3-18 month	Range: 3-18 months
Setting	Outpatient Treatment Centre BURTSCHEIDT2002 Inpatient MONTI1993 Homeless Soup Kitchen ROSENBLUM2005b	Inpatient ERIKSEN1986 JOHN2003 Outpatient Treatment Centre O'FARRELL1992 SELLMAN2001 WALITZER2009 Outpatient Research Unit LITT2003	Inpatient MONTI1990 Outpatient Treatment Centre BURTSCHEIDT2002 MARQUES2001 LITT2009 Outpatient Research Unit CONNORS2001 ROSENBLUM2005a
Treatment Goal	Not explicitly Stated BURTSCHEIDT2002 MONTI1993 ROSENBLUM2005b	Drinking Reduction/Moderation CONNORS2001 EASTON2007 MORGENSTERN2007 SANDAHL1998 SITHARTHAN1997 Abstinence OR drinking reduction/moderation DAVIDSON2007 ERIKSEN1986 MATCH1997 VEDEL2008[28] Not explicitly stated LAM2009 LITT2003 SHAKESHAFT2002 WALITZER2009	Drinking Reduction/Moderation CONNORS2001 Not explicitly stated BURTSCHEIDT2002 MARQUES2001 LITT2009 MONTI1990 ROSENBLUM2005a
	Cognitive Behavioural Therapies vs. TAU or Control	**Cognitive Behavioural Therapies vs. Other Active Intervention**	**Different formats of Cognitive Behavioural Therapy**

[28] Guidelines were stipulated for controlled drinking.

Country	BURTSCHEIDT2002 (Germany) MONTI1993 (USA) ROSENBLUM2005b (USA)	CONNORS2001 (USA) DAVIDSON2007 (USA) EASTON2007 (USA) ERIKSEN1986 (Norway) LAM2009 (USA) LITT2003 (USA) MATCH1997 (USA) MORGENSTERN2007 (USA) SANDAHL1998 (Sweden) SHAKESHAFT2002 (Australia) SITHARTHAN1997 (Australia VEDEL2008 (Netherlands WALITZER2009 (USA)	BURTSCHEIDT2002 (Germany) MARQUES2001 (Brazil) CONNORS (USA) LITT2009 (USA) MONTI1990 (USA) ROSENBLUM2005a (USA)

6.9.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Cognitive Behavioural Therapies versus TAU or control

Cognitive behavioural therapies were significantly better than control at reducing heavy drinking episodes but no significant difference between groups was observed for a reduction in days any alcohol is used (assessed post-treatment) or the number of participants who have lapsed and relapsed (assessed at 3 month follow-up) when compared to TAU. However, resulting in a moderate effect size, cognitive behavioural therapies were significantly better than TAU in reducing the number of participants who lapsed and relapsed when assessed at 6 month follow-up. No difference between groups was observed in attrition rates post-treatment or at 6 month follow-up.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate (see Appendix 18c for full GRADE profile).

Two studies assessing cognitive behavioural therapies versus control could not be added to the meta-analyses. KÄLLMÉN2003 could not be included as the data was presented in an unusable format. The study reported that the control group (unstructured discussion) drank significantly less alcohol at 18 month follow-up than the group receiving coping skills. ALLSOP1997 could not be included in analyses as it is not an RCT. The authors reported that relapse prevention treatment was significantly better than two control groups (an unstructured discussion and no treatment) in maintaining abstinence at 6 months and in the amount of time to first lapse or relapse. However, these effects were no longer significant at 12 month follow-up. An evidence summary of the results of the meta-analyses can be seen in Table 11.

Cognitive Behavioural Therapies versus other active intervention

Meta-analyses results revealed no significant difference between cognitive behavioural therapies and other therapies in maintaining abstinence both post-treatment and up to 15 month follow-up. A single study however did favour coping skills over counselling in the number of sober days at 12 month follow up, and another single study favouring relapse prevention over psychotherapy at 15 month follow-up. However, these single outcomes do not reflect the meta-analyses results described above. In addition, cognitive behavioural therapies were found to be more effective at maintaining abstinence/light days when assessed up to 18 month follow-up (based on data by CONNORS2001). No significant difference was observed between groups in reducing heavy drinking episodes and the amount of alcohol consumed both post-treatment and up to 18 month follow-up. A single study outcome (ERIKSEN1986) favoured coping skills over counselling in reducing the amount of alcohol consumed, but again, this single study was not reflective of other analyses with similar variables. Two studies assessing cognitive behavioural therapies versus another active intervention could not be included in analyses as they were non-RCTs. DAWE2002 compared moderation-oriented cue-exposure with

behavioural self-control training and reported no significant difference between groups in a variety of alcohol measures. LOEBER2006 also reported no significant between coping skills and cue exposure (behavioural treatment) in various drinking outcomes.

The VEDEL2008 study assessed severity of relapse in their sample. The results indicated that other active intervention (namely CBT) was more effective than couples therapy (namely BCT) in reducing occasions in which participants lapsed drank over six drinks on one occasion) or relapsed (drank more than six drinks most days of the week, but no significant difference was observed in the number of participants who relapsed on a regular basis (a few times a month). It must be noted that effect sizes were small and the results of a single study cannot be generalised.

No significant difference was observed between cognitive behavioural therapy and other active therapies in attrition rates.

The quality of this evidence is *high* therefore further research is unlikely to change our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 12 and Table 13.

Comparing different formats of cognitive behavioural therapies

For maintaining abstinence, an individual assessment treatment programme was significantly more effective than a packaged CBT program when assessed post-treatment (moderate effect size based on a single study). However, for the same comparison, no significant difference was observed between groups in reducing heavy drinking episodes. The additional of motivational enhancement to relapse prevention did not reduce the number of possible drinking days (at 6 month follow-up) and analyses favoured standard relapse prevention (moderate effect size). Furthermore, the addition of family therapy to coping skills did not show any significant benefit. Also, no significant difference in various drinking outcomes was observed between coping skills and other types of cognitive behavioural therapies (e.g. CBMMT) when assessed at 6 month follow-up. No difference between CBT and coping skills were observed in the number of participants who had lapsed or relapsed at 6 month follow-up. No difference in attrition rates were observed between the various types of cognitive behavioural therapy.

More intensive coping skills was significantly better than standard coping skills at maintaining abstinent/light drinking at 12 month follow-up (moderate effect size) but this benefit was no longer significant at 18 month follow-up. Individual cognitive behavioural therapy was significantly more effective than group cognitive behavioural therapy in reducing the number of heavy drinkers at 15 month follow-up.

The quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 14 and Table 15.

Table 40. Cognitive Behavioural Therapies vs. TAU or Control Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Rates of Consumption			

Rates of Consumption Post Treatment			
Number of Days any alcohol use	139	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-0.64, 0.03]
Number of Days Heavy alcohol use (>4 drinks)	46	Std. Mean Difference (IV, Random, 95% CI)	-0.70 [-1.30, -0.11]
Lapse or Relapse			
Lapsed - up to 6 months follow-up			
at 3 month follow-up	34	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.64, 2.54]
at 6 month follow-up	137	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.57, 0.99]
Relapse up to 6 month follow-up			
at 3 month follow up	30	Risk Ratio (M-H, Random, 95% CI)	1.57 [0.69, 3.59]
at 6 month follow up	133	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.38, 0.80]
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	324	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.74, 1.53]
Attrition (Drop-Out) up to 6 month follow-up			
at 3 month follow-up	32	Risk Ratio (M-H, Random, 95% CI)	Not estimable
at 6 month follow up	135	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.18, 1.54]

Table 41. Cognitive Behavioural Therapies vs. Other Interventions Evidence Summary (1)

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estima
Abstinence			
Abstinence Post Treatment			
Days abstinent	1901	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.21, 0.
Abstinence up to 6 month follow-up			
% Days Abstinent at 3 month follow-up	280	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.23, 0.
% Days Abstinent at 6 month follow-up	1946	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.12, 0.
Abstinence from 7-12 month follow-up			
% days abstinent at 9 months	1886	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.14, 0.
% Days Abstinent at 12 months	1887	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.12, 0.
Number of Sober Days at 12 month follow up	23	Std. Mean Difference (IV, Random, 95% CI)	-1.67 [-2.65, -0
Abstinence > 12 month follow-up			
% Days Abstinent at 15 month follow-up	1702	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.16, 0.
Number of Days abstinent at 15 month follow-up	44	Std. Mean Difference (IV, Random, 95% CI)	0.64 [0.03, 1.2
% Days Abstinent at 18 month follow-up	128	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.57, 0.
Abstinent/Light (1-3 standard drinks) up to 6 month follow up			
at 6 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.94 [-1.48, -0
Abstinent/Light (1-3 standard drinks) 7-12 month follow up			
at 12 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.84 [-1.40, -0
Abstinent/Light (1-3 standard drinks) >12 month follow up			
at 18 month follow-up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.74 [-1.26, -0
Lapse or Relapse			
Days to first drink at 18 month follow-up	128	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.20, 0.
Days to first heavy drinking day at 18 month follow-up	128	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.44, 0.
Relapse (>6 units most days of the week) Post Treatment	48	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.18, 0.8
Regular Relapse (>6 units a few times a month) Post Treatment	48	Risk Ratio (M-H, Random, 95% CI)	1.56 [0.44, 5.5
Severe lapse (>6 units on one occasion) Post Treatment	48	Risk Ratio (M-H, Random, 95% CI)	2.33 [1.01, 5.3
Rates of Consumption			
Rates of Consumption Post Treatment			

% heavy drinking days	149	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.37, 0.
Rate of consumption up to 6 month follow-up			
Proportion days heavy drinking at 3 month follow-up	280	Std. Mean Difference (IV, Random, 95% CI)	0.18 [-0.21, 0.5
Proportion days heavy drinking at 6 month follow-up	275	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.26, 0.5
Drinking days per month at 6 month follow-up	42	Std. Mean Difference (IV, Random, 95% CI)	0.61 [-0.01, 1.2
Binge consumption (occasions in prior 30 days where at least 7 (males) or 5 (females) drinks consumed at 6 month follow-up	115	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.38, 0.
Rate of consumption - 7-12 month follow-up			
Proportion days heavy drinking at 9 month follow-up	271	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.29, 0.
Proportion days heavy drinking at 12 month follow-up	267	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.25, 0.3
Rate of consumption > 12 month follow-up			
Days > 80 g of absolute alcohol at 15 month-follow-up	44	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.53, 0.6
Proportion days heavy drinking at 15 months	128	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.42, 0.
Proportion days heavy drinking at 18 months	190	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.50, 0.

Table 42. Cognitive Behavioural Therapies vs. Other Interventions Evidence Summary (2)

Outcome or Subgroup	Number of Participants	Statistical Method	
Amount of Alcohol Consumed			
Amount of alcohol consumed Post Treatment	1788	Std. Mean Difference (IV, Random, 95% CI)	0
Amount of alcohol consumed up to 6 month follow-up			
Number of participants consuming at hazardous/harmful levels weekly - at 6 month follow-up	295	Risk Ratio (M-H, Random, 95% CI)	1
Number of participants binge drinking had at least 12 binge episodes in previous 30 days - at 6 month follow-up	295	Risk Ratio (M-H, Random, 95% CI)	1
Number of participants binge drinking at all (at least 1 binge episode in previous 30 days) at 6 month follow-up	295	Risk Ratio (M-H, Random, 95% CI)	0
Units of alcohol per week at 5 month follow-up	48	Std. Mean Difference (IV, Random, 95% CI)	0
Units of alcohol per week at 6 month follow-up	45	Std. Mean Difference (IV, Random, 95% CI)	0
Drinks per occasion/drinking day at 6 months	1683	Std. Mean Difference (IV, Random, 95% CI)	0
Drinks per week at 6 months	115	Std. Mean Difference (IV, Random, 95% CI)	-0
Amount of alcohol consumed - 7-12 month follow-up			
Alcohol consumption (cl pure alcohol) at 12 month follow-up	24	Std. Mean Difference (IV, Random, 95% CI)	-1
Drinks per drinking day at 9 month follow up	1615	Std. Mean Difference (IV, Random, 95% CI)	-0
Drinks per drinking day at 12 month follow up	1683	Std. Mean Difference (IV, Random, 95% CI)	0
Amount of alcohol consumed > 12 month follow-up	1618	Std. Mean Difference (IV, Random, 95% CI)	-0
grams absolute alcohol per drinking day at 15 month follow-up	44	Std. Mean Difference (IV, Random, 95% CI)	-0
Drinks per drinking day at 15 month follow up	1574	Std. Mean Difference (IV, Random, 95% CI)	-0
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	2267	Risk Ratio (M-H, Random, 95% CI)	1
Attrition (Drop-Out) - up to 6 month follow-up			
at 3 month follow-up	200	Risk Ratio (M-H, Random, 95% CI)	1
at 6 month follow-up	2296	Risk Ratio (M-H, Random, 95% CI)	0
Attrition (Drop-Out) - 7 -12 month follow-up			
at 9 month follow-up	1788	Risk Ratio (M-H, Random, 95% CI)	1

at 12 month follow-up	1988	Risk Ratio (M-H, Random, 95% CI)	1
Attrition (Drop-Out) - >12 month follow up	1773	Risk Ratio (M-H, Random, 95% CI)	1
at 15 month follow up	1643	Risk Ratio (M-H, Random, 95% CI)	1
at 18 month follow-up	130	Risk Ratio (M-H, Random, 95% CI)	4

Table 43. Comparing Different Formats of Cognitive Behavioural Therapy Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estim
Abstinence			
Abstinence Post Treatment	110	Std. Mean Difference (IV, Random, 95% CI)	0.39 [0.01, 0
Abstinence up to 6 month follow up			
at 15 week follow-up	186	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-0.60, -
% possible drinking days (any day not in inpatient treatment or jail) abstinent at 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.52,
Abstinent/Light (1-3 standard drinks) Drinking Days up to 6 month follow up			
at 6 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.39 [-0.90,
Abstinent/Light (1-3 standard drinks) Drinking Days 7-12 month follow up			
at 12 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.65 [-1.21, -
Abstinent/Light (1-3 standard drinks) Drinking Days >12 month follow up			
at 18 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	-0.38 [-0.96,
Rates of Consumption			
Rates of Consumption Post Treatment			
Proportion of heavy drinking days (men>6, women>4 drinks)	110	Std. Mean Difference (IV, Random, 95% CI)	0.34 [-0.04, 0
Rates of Consumption up to 6 month follow up			
% of possible days (any day not in inpatient treatment or jail) heavy (>6) drinking at 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.65,
Rates of Consumption >12 month follow-up			
Number of Drinking Days at 15 month Follow-up	106	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.41,
Number of Problem Drinking days at 15 month follow-up	106	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.14, 0
Number of Heavy Drinking Days at 15 month follow-up	106	Std. Mean Difference (IV, Random, 95% CI)	0.37 [-0.01, 0
Amount of Alcohol Consumed			
Amount of Alcohol Consumed up until 6 month follow up			
Number of drinks per possible drinking day (any day not in inpatient treatment or jail) at 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	-0.30 [-0.73,
Number of drinks per actual drinking day at 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	-0.49 [-1.44,

Table 44. Comparing Different Formats of Cognitive Behavioural Therapy Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effec

Lapse or Relapse/ Other Outcomes			
Number of Participants Lapsed - up to 6 month follow-up	63	Risk Ratio (M-H, Random, 95% CI)	1.09
at 6 months	63	Risk Ratio (M-H, Random, 95% CI)	1.09
Number of Participants Relapse - up to 6 month follow-up	63	Risk Ratio (M-H, Random, 95% CI)	1.03
at 6 months	63	Risk Ratio (M-H, Random, 95% CI)	1.03
Number of days to 1st drink (lapse) up until 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	0.19 [
at 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	0.19 [
Number of days to first heavy drink (relapse) up until 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	0.11 [
at 6 month follow up	94	Std. Mean Difference (IV, Random, 95% CI)	0.11 [
Number Heavy Drinkers >20 drinks/wk and >10% heavy days (>=5 drinks/occasion) at 15 month follow-up	100	Risk Ratio (M-H, Random, 95% CI)	2.86
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	204	Risk Ratio (M-H, Random, 95% CI)	0.87
Attrition (Drop-Out) up to 6 month follow-up	515	Risk Ratio (M-H, Random, 95% CI)	1.07
at 15 week follow-up	230	Risk Ratio (M-H, Random, 95% CI)	1.11
at 6 months	285	Risk Ratio (M-H, Random, 95% CI)	0.99
Attrition (Drop-Out) 7-12 month follow up	132	Risk Ratio (M-H, Random, 95% CI)	0.89 [
at 12 month follow up	132	Risk Ratio (M-H, Random, 95% CI)	0.89 [
Attrition (Drop-Out) >12 month follow up	285	Risk Ratio (M-H, Random, 95% CI)	0.99
at 15 month follow up	155	Risk Ratio (M-H, Random, 95% CI)	0.87
at 18 month follow up	130	Risk Ratio (M-H, Random, 95% CI)	4.43 [

6.10 Behavioural Therapies (excluding contingency management)[29]

6.10.1 Definition

Behavioural interventions use behavioural theories of conditioning to help achieve abstinence from drinking by creating negative experiences/events in the presence of alcohol, and positive experiences/events in alcohols absence. Behavioural therapies considered for review included cue exposure, behavioural self-control training, aversion therapy and contingency management. Variants of two therapies (cue exposure and behavioural self-control training) which were based on a similar theoretical understanding of the nature of alcohol misuse were considered as single entity of the purposes of the review. Contingency management, although a behavioural intervention, was analysed separately because it is based on classic reinforcement model and has no alcohol specific formulation (see section 6.11 for evidence review). Aversion therapy was excluded because it is no longer routinely used in alcohol treatment in the UK.

Cue Exposure

Cue exposure treatment for alcohol misuse is based on both learning theory models and social learning theory and suggests that environmental cues associated with drinking can elicit conditioned responses which can in turn lead to a relapse (Niaura *et al*. 1988). The first case study using cue exposure treatment for excessive alcohol consumption was reported by Hodgson & Rankin (1976). Treatment is designed to reduce craving for alcohol by repeatedly exposing the service user to alcohol related

[29] See section 6.11 for a review of contingency management

cues until the service user 'habituates' to the cues and can hence maintain self-control in a real-life situation where these cues are present.

Behavioural self-control training

Behavioural self-control training is also referred to as 'behavioural self-management training' and is based on the techniques described by Miller and Muńoz (1976). Patients are taught to set limits for drinking, self-monitor drinking episodes, refusal skills training and training for coping behaviours in high-risk relapse situations. Behavioural self-control training is focused on a moderation goal rather than abstinence.

6.10.2 Clinical review protocol (Behavioural Therapies)

Information about the databases searched and the inclusion/ exclusion criteria used for this section of the guideline can be found in Appendix 16d (further information about the search for health economic evidence can be found in Section 6.21).

Table 45. Clinical review protocol for the review of Behavioural therapies.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Behavioural Self-Management, Behavioural Self-Management Training, Behavioural Self-Control Training, Cue Exposure (alone or with Cognitive Behavioural Therapy or Coping Skills), Moderation-Oriented Cue Exposure
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.10.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of behavioural therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 17 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Six RCT trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=527 participants. All six studies were published in peer-reviewed journals between 1988 and 2006. A number of studies identified in the

search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see Chapter 3). When studies did meet basic methodological inclusion criteria, the main reasons for exclusion were not having alcohol-focused outcomes that could be used for analysis, and not meeting drinking quantity/diagnosis criteria, i.e. participants were not drinking enough to be categorised as harmful or dependent drinkers or less than 80% of the sample meet criteria for alcohol dependence or harmful alcohol use. A list of excluded studies can be found in Appendix 16d.

Behavioural therapies versus control

Of the six included trials, there were two involving a comparison of behavioural therapies versus control which met criteria for inclusion. ALDEN1988 assessed behavioural self-management training versus waiting list control, and MONTI1993 assessed cue exposure with coping skills versus control (treatment-as-usual and daily cravings monitoring). The included studies were conducted between 1988 and 1993.

Behavioural Therapies versus other active intervention

Of the six included trials, four trials which evaluated behavioural therapies versus other active interventions met criteria for inclusion. Behavioural and other active therapies were as follows: ALDEN1988 (behavioural self-management versus developmental counselling); KAVANAGH2006 (cue exposure plus cognitive behavioural therapy versus emotional cue exposure plus cognitive behavioural therapy); SITHARTHAN1997 (cue exposure versus cognitive behavioural therapy); WALITZER2004 (behavioural self management versus behavioural couples therapy with alcohol focused spousal involvement and alcohol focused spousal involvement alone). The included studies were conducted between 1988 and 2006.

Comparing different formats of behavioural therapy

Of the six included trials, two trials which assessed one type of behavioural therapy versus another met criteria for inclusion. The behavioural therapies in the HEATHER2000 study were moderation-oriented cue exposure and behavioural self-control training. In the KAVANAGH2006 study, they were cue exposure (plus cognitive behavioural therapy) and emotional cue exposure (plus cognitive behavioural therapy). The included studies were conducted between 2000 and 2006.

Table 46. Summary of study characteristics for Behavioural Therapies

	Behavioural Therapies vs. Control/TAU	Behavioural Therapies vs. Other Active Intervention	Different formats of behavioural therapy
***K*(total N)**	2(134)	4(3420	2(199)
Study ID	ALDEN1988 MONTI1993	ALDEN1988 KAVANAGH2006 SITHARTHAN1997 WALITZER2004	HEATHER2000 KAVANAGH2006
Diagnosis (when reported)	DSM alcohol dependent MONTI1993	DSM alcohol dependent KAVANAGH2006 85% had low level alcohol dependence and 15% had moderate levels WALITZER2004	DSM alcohol dependen KAVANAGH2006
Baseline severity	ALDEN1988 *Consuming >84 standard ethanol units per week* MONTI1993 *-ADS score: 20.7* *-SMAST score: 9.97* *-Drinks/drinking day: 12.1; abstinent days: 47%; heavy drinking days: 45%*	ALDEN1988 *Consuming >84 standard ethanol units per week* KAVANAGH2006 *- SADQ-C score: approx 13.7* *-AUDIT score: approx 28* *-Weekly alcohol consumption: approx 37* SITHARTHAN1997 *-SADQ-C score: 18.81* *-ICQ score: 13.05* *-CDSES score: 35.93* *-Drinking days/ month: 20.2; consumption/ occasion: 8.82* WALITZER2004 *-ADS score: 8.4* *-Abstinent days/month: 11.0; Frequency of >6 drink per drinking period per month: 5.1*	HEATHER2000 *-SADQ-C score: 18.7* *-APQ: 10.1* *-Drinks/drinking day: 19.96; abstinent days: 19.14%* KAVANAGH2006 *- SADQ-C score: approx* *-AUDIT score: approx 28* *-Weekly alcohol consump approx 37*
Number of sessions	Range: 6-12	Range: 6-12	8 sessions
Length of treatment	Range: 6-12 weeks	Range: 6-12 weeks	8 weeks
Length of Follow-up	Range: 6-24 months	Range: 3-12 months	Range: 3-12 months
Setting	Inpatient VA Medical Centre MONTI1993 Outpatient Clinical Research Unit ALDEN1988	Outpatient Clinical Research Unit ALDEN1988 KAVANAGH2006 SITHARTHAN1997 WALITZER2004	Outpatient Clinical Research Unit HEATHER2000 KAVANAGH2006
Treatment Goal	Drinking Reduction/Moderation ALDEN1988 Not explicitly Stated MONTI1993	Drinking Reduction/Moderation ALDEN1988 KAVANAGH2006 SITHARTHAN1997 WALITZER2004	Drinking Reduction/Moderation HEATHER2000 KAVANAGH2006
Country	ALDEN1988 (Canada) MONTI1993 (USA)	ALDEN1988 KAVANAGH2006 (Australia) SITHARTHAN1997 (Australia) WALITZER2004 (USA)	HEATHER2000 (UK) KAVANAGH2006 (Austra

6.10.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Behavioural therapies versus control/TAU

The review evidence indicated behavioural therapies were more effective than control in reducing the amount of alcohol consumed (SMD=-0.97, large effect size) and maintaining controlled drinking (SMD=-0.60, medium effect size) when assessed post treatment. However, it must be noted that this was based on a single study.

No significant difference was observed between behavioural therapies and control in maintaining abstinence when assessed post treatment. Furthermore, no significant difference could be found between behavioural therapies and control in the number of participants who lapsed or relapsed up to 6 month follow-up. In addition, there was no significant difference between behavioural therapies and control in attrition rates.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 18.

Behavioural therapy versus other active intervention

The review evidence indicated that behavioural therapies were not as effective as other interventions (in this case couples-based therapies) in maintaining abstinent/light drinking days up to 12 month follow-up. In addition to this, there was no significant difference between behavioural therapies and counselling in maintaining abstinence both post treatment and up to 24 month follow-up.

No difference was observed between behavioural therapies and other active interventions (e.g. CBT) in reducing the amount of alcohol consumed up to 24 month follow up. However, one study (SITHARTHAN1997) showed a medium effect size favouring cue exposure over CBT in reducing drinks per occasion at 6 month follow-up.

Behavioural therapies were not as effective as other active interventions (namely couples therapies) in reducing heavy drinking days. Medium to high effects favouring couples therapy were found at all assessment points up to 12 month follow-up.

The review results revealed that other therapies (i.e. CBT and counselling) had significantly less post-treatment attrition than behavioural therapies. However, no significant difference was observed between treatments at follow-up (3-24 months).

Three trials with inadequate randomisation assessing cue exposure versus another active intervention could not be included in analyses. DAWE2002 and LOEBER2006 reported no significant difference between cue exposure and another active intervention (behavioural self-control training and coping skills respectively) for various alcohol outcomes. However, DRUMMOND1994 found that cue exposure was more effective than a relaxation therapy in time to relapse and total alcohol consumption.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 19.

Comparing different formats of behavioural therapy

The clinical evidence indicates that there was no significant difference between cue exposure and behavioural self-control training in maintaining abstinence post treatment or at 6 month follow-up. Furthermore, no significant difference was observed between cue exposure and emotional cue exposure in reducing the amount of alcohol consumed at six to 12 month follow-up. In line with this, no significant difference was observed between moderation-oriented cue exposure and behaviour self-control training in reducing alcohol consumption when assessed at 6 month follow-up.

No difference was observed between behavioural therapies in attrition both at post-treatment and 6 month follow-up.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 20.

Table 47. Behavioural Therapy vs. TAU or control evidence summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinent Days Per Week Post Treatment	94	Std. Mean Difference (IV, Random, 95% CI)	-0.37 [-0.79, 0.04]
Amount of Alcohol Consumed			
Total Weekly Consumption Post Treatment	94	Std. Mean Difference (IV, Random, 95% CI)	-0.97 [-1.40, -0.54]
Lapse or Relapse			
Lapse Up to 6 Month Follow Up			
0-3 months	34	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.64, 2.54]
3-6 months	34	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.29, 1.10]
Relapse Up to 6 Month Follow Up			
at 0-3 months	34	Risk Ratio (M-H, Random, 95% CI)	1.60 [0.68, 3.79]
at 3-6 months	34	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.25, 1.61]
Rates of Consumption			
Controlled (<= 3 standard drinks) per week at Post Treatment	94	Std. Mean Difference (IV, Random, 95% CI)	-0.60 [-1.02, -0.18]
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	34	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.04, 4.45]
Attrition (Drop-Out) up to 6 Month Follow Up			
at 3 months	32	Risk Ratio (M-H, Random, 95% CI)	Not estimable
at 6 months	32	Risk Ratio (M-H, Random, 95% CI)	3.95 [0.20, 76.17]

Table 48. Behavioural Therapy vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinence Post Treatment			

% days abstinent per week	73	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.35, 0.57]
Controlled (<=3 standard drinks) per week Post Treatment	73	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.46, 0.47]
Abstinence up to 6 month follow up			
% Days Abstinent/Light per Month at 3 month Follow Up	63	Std. Mean Difference (IV, Random, 95% CI)	0.77 [0.23, 1.31]
% Days Abstinent/Light per Month at 6 month Follow Up	83	Std. Mean Difference (IV, Random, 95% CI)	0.49 [0.06, 0.93]
Abstinence 7-12 Month Follow Up			
% Days Abstinent/Light per Month at 9 month Follow Up	61	Std. Mean Difference (IV, Random, 95% CI)	0.60 [0.05, 1.15]
% Days Abstinent/Light per Month at 12 month Follow Up	61	Std. Mean Difference (IV, Random, 95% CI)	0.54 [-0.01, 1.09]
Abstinent Days per week at 12 month Follow Up	105	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.17, 0.60]
Controlled (<=3 standard drinks) per week at 12 Month Follow Up	105	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.19, 0.57]
Abstinence >12 month Follow Up			
Abstinent days per week at 24 month Follow Up	93	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.26, 0.55]
Controlled (<=3 standard drinks) per week at 24 Month Follow Up	93	Std. Mean Difference (IV, Random, 95% CI)	0.28 [-0.13, 0.69]
Amount of Alcohol Consumed			
Amount of Alcohol Consumed Post Treatment	73	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.59, 0.34]
Total Weekly Alcohol Consumption (standard drinks) Post Assessment	73	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.59, 0.34]
Amount of Alcohol Consumed Up to 6 Month Follow Up			
Total Weekly Alcohol Consumption at 3 month Follow Up	164	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.21, 0.44]
Drinks per occasion at 6 month Follow Up	42	Std. Mean Difference (IV, Random, 95% CI)	-0.66 [-1.29, -0.04]
Total Weekly Alcohol Consumption at 6 month Follow Up	164	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.19, 0.46]
Amount of Alcohol Consumed Per Week 7-12 Month Follow Up			
Total Weekly Alcohol Consumption at 9 month Follow Up	164	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.28, 0.37]
Total Weekly Alcohol Consumption at 12 month Follow Up	269	Std. Mean Difference (IV, Random, 95% CI)	0.18 [-0.07, 0.42]
Amount of Alcohol Consumed Per Week >12 Month Follow Up	105	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.31, 0.46]
Total Weekly Alcohol Consumption at 24 Months Follow Up	105	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.31, 0.46]
Rates of Consumption			
Rates of Consumption Up to 6 Month Follow Up			
% Days Heavy Drinking (>6 drinks per day) at 3 month Follow Up	64	Std. Mean Difference (IV, Random, 95% CI)	0.96 [0.42, 1.51]
% Days Heavy Drinking (>6 drinks per day) at 6 month Follow Up	63	Std. Mean Difference (IV, Random, 95% CI)	0.59 [0.06, 1.13]

Drinking Days Per Month at 6 month Follow Up	42	Std. Mean Difference (IV, Random, 95% CI)	-0.61 [-1.23, 0.01]
Rates of Consumption Up to 7-12 Month Follow Up			
% Days Heavy Drinking (>6 drinks per day) at 9 month Follow Up	62	Std. Mean Difference (IV, Random, 95% CI)	0.85 [0.30, 1.41]
% Days Heavy Drinking (>6 drinks per day) at 12 month Follow Up	62	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.12, 1.21]
2.11 Attrition (Drop-Out) Post Treatment	306	Risk Ratio (M-H, Random, 95% CI)	1.73 [1.13, 2.63]
2.12 Attrition (Drop-Out) Up to 6 Month Follow Up			
2.12.1 at 3 months	64	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.03, 13.87]
2.12.2 at 6 month	110	Risk Ratio (M-H, Random, 95% CI)	1.55 [0.35, 6.82]
Attrition (Drop-Out) 7-12 Month Follow Up	251	Risk Ratio (M-H, Random, 95% CI)	1.49 [0.72, 3.07]
at 9 months	63	Risk Ratio (M-H, Random, 95% CI)	3.10 [0.41, 23.61]
at 12 months	188	Risk Ratio (M-H, Random, 95% CI)	1.34 [0.61, 2.90]
Attrition (Drop-Out) >12 Month Follow Up	105	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.34, 2.85]
at 24 months	105	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.34, 2.85]

Table 49. Comparing Various Formats of Behavioural Therapy Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinent Post Treatment (MOCE vs BSCT)	77	Std. Mean Difference (IV, Random, 95% CI)	-0.23 [-0.68, 0.22]
Abstinence Up to 6 Month Follow Up			
at 6 Month Follow Up (MOCE vs BSCT)	91	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.19, 4.21]
Amount of Alcohol Consumed			
Amount of Alcohol Consumed Up to 6 Month Follow Up			
at 3 month Follow Up (CE vs. ECE)	108	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.40, 0.36]
at 6 month Follow Up (CE vs. ECE)	108	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.43, 0.33]
Amount of Alcohol Consumed 7-12 Months Follow Up			
Drinks per drinking day at 6 month Follow Up (MOCE vs BSCT)	77	Std. Mean Difference (IV, Random, 95% CI)	0.41 [-0.04, 0.86]
Amount of Alcohol Consumed at 9 months (CE vs. ECE)	108	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.39, 0.37]
Amount of Alcohol Consumed at 12 month Follow Up (CE vs. ECE)	108	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.40, 0.36]
Attrition (Drop-Out)			

Attrition (Drop-Out) Post Treatment (CE vs. ECE)	108	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.50, 1.14]
Attrition (Drop-Out) Up to 6 Month Follow Up at 6 Month Follow Up (MOCE vs. BSCT)	91	Risk Ratio (M-H, Random, 95% CI)	1.61 [0.59, 4.44]

6.11 Contingency Management

6.11.1 Definition

Contingency management provides a system of reinforcement designed to make continual alcohol use less attractive and abstinence more attractive. There are four main methods of providing incentives:

- Voucher-based reinforcement: People who misuse alcohol receive vouchers with various monetary values (usually increasing in value after successive periods of abstinence) for providing biological samples (usually urine) that are negative for alcohol. These vouchers are withheld when the biological sample indicates recent alcohol use. Once earned, vouchers are exchanged for goods or services that are compatible with an alcohol-free lifestyle.
- Prize-based reinforcement: This is more formally referred to as the 'variable magnitude of reinforcement procedure' (Prendergast *et al.*, 2006). Participants receive draws, often from a number of slips of paper kept in a fishbowl, for providing a negative biological specimen. Provision of a specimen indicating recent alcohol use results in the withholding of draws. Each draw has a chance of winning a 'prize', and the value of which varies. Typically, about half the draws say 'Good job!'. The other half results in the earning of a prize, which may range in value from £1 to £100 (Prendergast *et al.*, 2006).
- Cash incentives: people who misuse alcohol receive cash (usually of a relatively low value, for example, £1.50–£10) for performing the target behaviour, such as submitting a urine sample negative for alcohol or compliance with particular interventions. Cash incentives are withheld when the target behaviour is not performed.
- Clinic privileges: participants receive clinic privileges for performing the target behaviour, for example, providing a negative biological sample. But these privileges are withheld when the target behaviour is not performed. An example of a clinic privilege is a take-home methadone dose (for example, Stitzer *et al.*,1992). This incentive is appropriate for drug treatment for substances such as heroin but is not applicable to alcohol treatment.

6.11.2 Clinical review protocol (Contingency Management)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 50. Clinical review protocol for the review of Contingency Management.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Contingency Management
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.11.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of contingency management in the treatment of alcohol dependence or harmful alcohol use. See Table 22 for a summary of the study characteristics.

Three trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=355 participants. All three studies were published in peer-reviewed journals between 2000 and 2007. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was that the participants in the study did not meet drinking quantity/diagnosis criteria, i.e. participants were not drinking enough to be categorised as harmful or dependent drinkers or less than 80% of the sample meet criteria for alcohol dependence or harmful alcohol use. Another reason was that the study was drugs focused or did not differentiate between drugs and alcohol. A list of excluded studies can be found in Appendix 16d.

Contingency management versus control

Of the three included trials, there was only one involving a comparison of contingency management versus control which met criteria for inclusion. LITT2007 assessed contingency management with network support versus case management (control).

Contingency management versus TAU

Of the three included trials, two trials evaluating contingency management versus treatment-as-usual (standard care) met criteria for inclusion. Both ALESSI2007 and PETRY2000 assessed contingency management with standard care versus standard care alone. The included studies were conducted between 2000 and 2007.

Contingency Management versus other active intervention

Of the three included trials, one trial which assessed contingency management versus another active intervention met criteria for inclusion. The treatment conditions in LITT2007 were contingency management with network support versus network support alone.

Table 51. Summary of study characteristics for Contingency Management

	Contingency Management vs. Control	Contingency Management vs. Treatment-as-usual	Contingency Management vs. Other Active Intervention
***K*(total N)**	1(139)	2(145)	1(141)
Study ID	LITT2007	ALESSI2007 PETRY2000	LITT2007
Diagnosis (when reported)	DSM alcohol dependent/abuse LITT2007	DSM alcohol dependent/abuse ALESSI2007 DSM alcohol dependent PETRY2000)	DSM alcohol dependent/abuse LITT2007
Baseline severity	LITT2007 *-Drinking Days in past 3 months: 72%*	PETRY2000 *-Years of alcohol dependence: 23.5 years*	LITT2007 *-Drinking Days in past 3 months: 72%*
Number of sessions	12 sessions	CM: rewards for negative sample (ALESSI2007; PETRY2000) and attendance (ALESSI2007)	12 sessions
Length of treatment	12 weeks	N/A	12 weeks
Length of Follow-up	27 months	Range: Post-Treatment only	27 months
Setting	Outpatient Treatment Centre LITT2007	Outpatient Treatment Centre ALESSI2007 PETRY2000	Outpatient Treatment Centre LITT2007
Treatment Goal	Not explicitly Stated LITT2007	Abstinence ALESSI2007 PETRY2000	Not explicitly Stated LITT2007
Country	All USA	All USA	All USA

6.11.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Contingency Management versus control

The review evidence indicated that contingency management (with network support) was more effective at maintaining abstinence than control post treatment (large effect size) and up to 15 month follow up (medium effect size). However, no significant differences were observed between contingency management with network support and control for follow-up periods greater than 15 months. It should be noted that this analyses was based on the LITT2007 study only.

Contingency management (with network support) was more effective than control (low to medium effect size) at reducing drinking quantity when assessed at 6, 9 and 21 month follow-up. However, no significant difference was found between treatment conditions post treatment, at 12, 15, 18, 24 and 27 month follow-up.

No significant difference was observed between conditions in attrition either post-treatment and at all follow up points up to 27 months.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 23.

Contingency Management versus TAU (standard care)

The clinical review revealed no significant beneficial effect of adding contingency management to standard care in maintaining abstinence when assessed post treatment. However, the addition of contingency management to standard care was beneficial in reducing the number of participants who relapsed to heavy drinking. Furthermore, the addition of contingency management to standard care was beneficial in reducing attrition rates.

The quality of this evidence is moderate therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 24.

Contingency management versus other active intervention

The addition of contingency management to network support was not beneficial in maintaining abstinence both post-treatment and up to 9 month follow-up. However, network support without contingency management was more effective at maintaining abstinence at 12 to 24 month follow-up.

The quality of this evidence is moderate therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 25.

Table 52. Contingency Management vs. Control Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinence Post Treatment			
% Days Abstinent Post Treatment	114	Std. Mean Difference (IV, Random, 95% CI)	-0.80 [-1.18, -0.42
Abstinence up to 6 month follow up			
at 6 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.06, -0.31
Abstinence 7-12 month Follow Up			
at 9 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.58 [-0.96, -0.21
at 12 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.39 [-0.76, -0.02
Abstinence > 12 month Follow Up			
at 15 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.50 [-0.87, -0.12
at 18 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.27, 0.47]
at 21 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.52, 0.22]
at 24 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.61, 0.12]
at 27 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.27, 0.46]
Amount of Alcohol Consumed			

Amount of Alcohol Consumed (DDD) Post Treatment	114	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.61, 0.12]
Amount of Alcohol Consumed (DDD) up to 6 Month Follow Up	114		
at 6 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.66 [-1.04, -0.28]
Amount of Alcohol Consumed (DDD) 7-12 Month Follow Up			
at 9 months	114	Std. Mean Difference (IV, Random, 95% CI)	-0.38 [-0.75, -0.01]
at 12 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.47, 0.26]
Amount of Alcohol Consumed (DDD) >12 Month Follow Up			
at 15 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.48, 0.26]
at 18 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.63, 0.11]
at 21 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.53 [-0.90, -0.16]
at 24 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.47, 0.27]
at 27 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.23, 0.50]
Attrition (Drop-Out)			
Attrition (Drop-out) Post Treatment	139	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.35, 4.40]
Attrition (Drop-out) up to 6 month follow up			
at 6 months	130	Risk Ratio (M-H, Random, 95% CI)	2.00 [0.19, 21.52]
Attrition (Drop-out) 7-12 month Follow Up			
at 9 months	127	Risk Ratio (M-H, Random, 95% CI)	7.11 [0.37, 134.89]
at 12 months	124	Risk Ratio (M-H, Random, 95% CI)	Not estimable
Attrition (Drop-out) > 12 Month Follow Up			
at 18 months	123	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.07, 16.95]
at 27 months	117	Risk Ratio (M-H, Random, 95% CI)	2.18 [0.20, 23.37]

Table 53. Contingency Management vs. Standard Care (TAU) Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinence Post Treatment			
Longest duration abstinent (weeks) Post Treatment	103	Std. Mean Difference (IV, Random, 95% CI)	-0.27 [-0.66, 0.12]
Lapse or Relapse			
Number relapsed to heavy drinking at end of treatment	42	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.19, 0.98]
Number Lapsed (non-abstinent) at the end of treatment	42	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.25, 1.09]
Attrition (Drop-Out)			
Attrition (Drop-out) abstinence Post Treatment	145	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.07, 0.52]

Table 54. Contingency Management vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinence Post Treatment			
% Days Abstinent Post Treatment	112	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.49, 0.25]
Abstinence up to 6 Month Follow Up			
at 6 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.24, 0.50]
Abstinence 7-12 month Follow Up			
at 9 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.18, 0.56]
at 12 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.37 [-0.00, 0.75]
Abstinence > 12 month Follow Up			
at 15 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.35 [-0.02, 0.72]
at 18 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.70 [0.32, 1.08]
at 21 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.37 [-0.01, 0.74]
at 24 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.11, 0.86]
at 27 month follow up	112	Std. Mean Difference (IV, Random, 95% CI)	0.84 [0.45, 1.22]

Amount of Alcohol Consumed			
Amount of Alcohol Consumed (DDD) Post Treatment	114	Std. Mean Difference (IV, Random, 95% CI)	-0.36 [-0.73, 0.01]
Amount of Alcohol Consumed (DDD) up to 6 Month Follow Up			
at 6 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.62, 0.12]
Amount of Alcohol Consumed (DDD) 7-12 Month Follow Up			
at 9 months	114	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.42, 0.31]
at 12 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.32 [-0.05, 0.69]
Amount of Alcohol Consumed (DDD) >12 Month Follow Up			
at 15 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.49 [0.12, 0.87]
at 18 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.20, 0.54]
at 21 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.57, 0.16]
at 24 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.34, 0.40]
at 27 month follow up	114	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.22, 0.52]
Attrition			
Attrition (Drop-out) Post Treatment	141	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.27, 2.64]
Attrition (Drop-out) up to 6 month follow up			
at 6 months	130	Risk Ratio (M-H, Random, 95% CI)	5.00 [0.24, 102.16]
Attrition (Drop-out) 7-12 month Follow Up			
at 9 months	128	Risk Ratio (M-H, Random, 95% CI)	3.10 [0.33, 28.97]
at 12 months	124	Risk Ratio (M-H, Random, 95% CI)	Not estimable
Attrition (Drop-out) > 12 Month Follow Up			
at 18 months	122	Risk Ratio (M-H, Random, 95% CI)	3.20 [0.13, 77.04]
at 27 months	117	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.13, 4.19]

6.12 Social Network and Environment Based Therapies

6.12.1 Definition

Social network and environment based therapies use the individual's social environment as a way to help achieve abstinence or controlled drinking. These therapies include social behaviour and network therapy (SBNT) and the community reinforcement approach (CRA).

Social behaviour and network therapy (SBNT)

Social behaviour and network therapy (SBNT) comprises a range of cognitive and behavioural strategies to help clients build social networks supportive of change which involve the patient and members of the patient's networks (e.g. friends and family) (Copello, 2002). The integration of these strategies has the aim of helping the patient to build 'positive social support for a change in drinking'.

The Community Reinforcement Approach (CRA)

In the community reinforcement approach (Hunt & Azrin, 1973; Meyers & Miller, 2001; Sisson & Azrin, 1989), emphasis is placed on maintaining abstinence through the development of activities that do not promote alcohol use, e.g. recreational and social activities, employment and family involvement.

6.12.2 Clinical review protocol (Social Network and Environment Based Therapies)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 55. Clinical review protocol for the review of Social Network and Environment Based Therapies.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Social Network and Environment Based Therapies
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.12.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of social network and environment based therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 27 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Three trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=1058 participants. All three studies were published in peer-reviewed journals between 1999 and 2007. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was not having alcohol-focused outcomes that could be used for analysis. A list of excluded studies can be found in Appendix 16d.

Social Network and Environment Based Therapies versus control

Of the three included trials, there was only one involving a comparison of social network and environment based therapies versus control which met criteria for inclusion. LITT2007 assessed network support (both with and without contingency management) versus a case management control. In this study, network support involved encouraging the participant to change their social network form one that

promotes drinking to one that encourages abstinence as well as encouraging the use of established social support networks such as alcoholics anonymous (AA).

Social Network and Environment Based Therapies versus Other Active Intervention

Two of the three included trials which met criteria for inclusion assessed social network and environment based therapies versus another active intervention. LEIGH1999 investigated a volunteer support condition (a volunteer was part of most treatment sessions and spent a substantial amount of time with the participant whilst in the community) versus an unspecified office-based individual intervention. UKATT2005 investigated social behaviour and network therapy (see Section 6.12.1 for definition) versus motivational enhancement therapy.

Table 56. Summary of study characteristics for Social Network and Environment Based Therapies

	Social Network and Environment Based Therapies vs. Control	Social Network and Environment Based Therapies vs. Other Active Intervention
***K*(total N)**	1(210)	2(989)
Study ID	LITT2007	LEIGH2009 UKATT2005
Diagnosis (when reported)	DSM alcohol dependent/abuse LITT2007	DSM alcohol dependent/abuse UKATT2005
Baseline severity	LITT2007 *-Drinking days in past 3 months: 72%* *-Prior treatment for alcohol dependence: 1.3*	LEIGH1999 *-Outpatient alcoholics drinking 5.5 days per week* *-Drinks/week: Range 73-89* UKATT *-Days abstinent: 29.5% per month* *-Number of drinks/drinking day: 26.8*
Number of sessions	12 sessions	8 sessions
Length of treatment	12 weeks	Range: 8 – 16 weeks
Length of Follow-up	6-27 month	Range: 1-12 month
Setting	Outpatient Treatment Centre LITT2007	Outpatient Treatment Centre LEIGH1999 UKATT2005
Treatment Goal	Not explicitly Stated LITT2007	Abstinence OR Drinking Reduction/Moderation LEIGH1999 UKATT2005
Country	LITT2007 (USA)	LEIGH2009 (Canada) UKATT2005 (UK)

6.12.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Social Network and Environment Based Therapies versus ***Control***

The clinical evidence showed that social network and environment based therapies were significantly better than control at maintaining abstinence (moderate effect size)

when assessed post treatment, and at 6, 9, 12, 15 and 24 month follow-up. However, no significant difference was observed at 18, 21 and 27 month follow-up.

Social network and environment based therapies were not significantly better than control in reducing drinking at post treatment or at 12, 15, 24 and 27 month follow-up. However, a significant benefit (low to moderate effect size) was observed for social network and environment based therapies over control in reducing the quantity of alcohol consumed when assessed at 6, 9, 18 and 21 month follow-up.

No significant difference was observed between treatment conditions in attrition either post treatment or at all follow up points. It must be noted that the comparison between social network and environment based therapies versus control was based on a single study.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 28.

Social Network and Environment Based Therapies versus ***other active intervention***

The clinical evidence did not reveal any significant difference between social network and environment based therapies and other active interventions in maintaining abstinence, reducing the quantity of alcohol consumed, reducing the number of drinking days and attrition.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 29.

Table 57. Social Network/Environment Based Therapies vs. Control Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinence Post Treatment			
% days Abstinent Post Treatment	172	Std. Mean Difference (IV, Random, 95% CI)	-0.76 [-1.08, -0.43]
Abstinence up to 6 month follow up			
at 6 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.75 [-1.08, -0.43]
Abstinence 7-12 month follow up			
at 9 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.70 [-1.03, -0.38]
at 12 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-0.99, -0.19]
Abstinence >12 month follow up			
at 15 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.03, -0.32]
at 18 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-1.02, 0.46]
at 21 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-0.74, 0.05]
at 24 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.49 [-0.96, -0.01]
at 27 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-1.12, 0.49]
Amount of Alcohol Consumed			
Drinks per Drinking Day Post Treatment	172	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.41, 0.28]
Drinks per Drinking Day up to 6 Month Follow Up			
at 6 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-0.86, -0.22]
Drinks per Drinking Day 7-12 Month Follow Up			
at 9 months	172	Std. Mean Difference (IV, Random, 95% CI)	-0.37 [-0.68, -0.05]

at 12 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.57, 0.06]
Drinks per Drinking Day >12 Month Follow Up			
at 15 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-0.83, 0.12]
at 18 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.34 [-0.66, -0.03]
at 21 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.43 [-0.75, -0.11]
at 24 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.43, 0.20]
at 27 month follow up	172	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.26, 0.37]
Attrition (Drop-Out)			
Attrition (Drop-out) Post Treatment	211	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.45, 4.13]
Attrition (Drop-out) up to 6 month follow up			
at 6 months	196	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.08, 3.59]
Attrition (Drop-out) 7-12 month follow up			
at 9 months	192	Risk Ratio (M-H, Random, 95% CI)	2.41 [0.28, 20.76]
at 12 months	188	Risk Ratio (M-H, Random, 95% CI)	Not estimable
Attrition (Drop-out) >12 month follow up	365	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.22, 2.79]
at 18 months	186	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 2.64]
at 27 months	179	Risk Ratio (M-H, Random, 95% CI)	1.31 [0.26, 6.61]

Table 58. Social Network/Environment Based Therapies vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Abstinence up to 6 Month Follow Up			
% Days Abstinent at 3 month Follow-up	686	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.17, 0.13]
Abstinence 7-12 Month Follow Up			
% Days Abstinent at 12 month Follow-up	612	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.18, 0.14]
Rates of Consumption			
Rate of Consumption Up to 6 Month Follow Up			
Number Drinking Days at 1 month Follow Up	79	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.47, 0.41]
Number of Drinking Days 6 month Follow-up	79	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.35, 0.54]
Rate of Consumption at 7-12 Month Follow Up			
Number of Drinking Days 12 month Follow-up	79	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.29, 0.60]
Amount of Alcohol Consumed			
Amount of Alcohol Consumed Up to 6 Month Follow Up			
Mean Quantity per day at 1 month Follow Up	79	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.42, 0.46]
Mean Quantity/day 6 months Follow-up	79	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.02, 0.87]
Number Drinks per drinking day at 3 month Follow-up	624	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.12, 0.20]
Amount of Alcohol Consumed 7-12 Month at Follow Up	599	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.09, 0.23]
Mean Quantity/day 12 month Follow-up	79	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.31, 0.57]
Number of Drinks per drinking day at 12 month Follow-up	520	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.11, 0.23]
Attrition (Drop-Out)			
Attrition (Drop-out) Post Treatment	193	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.68, 1.28]
Attrition (Drop-out) up to 6 Month Follow Up			
at 3 month follow up	762	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.42, 1.08]
Attrition (Drop-out) 7-12 month follow up			
at 12 month follow up	689	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.65, 1.56]

6.13 Couples Therapy

6.13.1 Definition

The content and definition of couples therapy can vary and reflect different approaches, e.g. cognitive behavioural or psychodynamic. Couples-based interventions (including behavioural couples therapy [BCT]) involve the spouse or partner expressing active support for the person who misuses alcohol in reducing alcohol use, including via the use of behavioural contracts. Couples are helped to improve their relationship through more effective communication skills, and encouraged to increase positive behavioural exchanges through acknowledgement of pleasing behaviours and engagement in shared recreational activities (Fals-Stewart et al., 2005). Standard BCT is manual based and structured (Fals-Stewart et al., 2004) and combines cognitive-behaviour treatment strategies with methods that address relationship issues arising from alcohol misuse as well as more general relationship problems with the aim of reducing distress.

6.13.2 Clinical review protocol (Couples Therapy)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 59. Clinical review protocol for the review of Couples Therapy.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Couples Therapy
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.13.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of couples therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 31 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Eight trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=602 participants. All eight studies were published in peer-reviewed journals between 1988 and 2009. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was not having alcohol-focused outcomes that could be used for analysis. Other reasons were not meeting drinking quantity/diagnosis criteria, i.e. participants were not drinking enough to be categorised as harmful or dependent drinkers or less than 80% of the sample meet criteria for alcohol dependence or harmful alcohol use, the study was outside the scope of this guideline, or the study was drugs focused or did not differentiate between drugs and alcohol. A list of excluded studies can be found in Appendix 16d.

Couples therapy versus other active intervention

Of the eight included RCT trials, seven compared couples therapy with another active intervention met criteria for inclusion. In the FALSSTEWART2005 study, participants received one of two methods of couples therapy (BCT and brief relationship counselling) or individually based TSF or psychoeducational intervention. All groups also had group counselling as standard. FALSSTEWART2006 assessed BCT (with individual TSF) versus individual TSF or psychoeducational intervention alone. LAM2009 investigated BCT (both with and without parental skills training) versus individually-based coping skills. OFARRELL1992 assessed two methods of couples therapy (interactional couples therapy and behavioural marital therapy) versus counselling. SOBELL2000 compared couples therapy in the form of direct social support with natural social support. VEDEL2008 compared BCT with CBT. WALITZER2004 investigated BCT with and without alcohol-focused spousal involvement with behavioural self-management.

Behavioural Couples Therapy versus Other Couples Therapy

Three studies assessed BCT versus other methods of couples therapy. Studies that could be included in these analyses compared BCT to the following; brief relationship therapy (FALSSTEWART2005), interactional couples therapy (OFARRELL1992), and alcohol focused spousal involvement (WALITZER2004).

Intensive Behavioural Couples Therapy versus Brief Couples Therapy

Two studies were included to assess the possible difference in outcome between more intensive and less intensive couples therapy. FALSSTEWART2005 assessed BCT (plus counselling) versus brief relationship therapy plus counselling (brief BCT). ZWEBEN1988 assessed eight sessions of conjoint therapy versus one session of couples advice counselling.

Parental Skills & Behavioural Couples Therapy versus Behavioural Couples Therapy alone

This analyses involved a single study (LAM2009) which assessed BCT with and without the addition of parental skills training.

Table 60. Summary of study characteristics for Couples Therapy

	Couples Therapy vs. Other Active Intervention	BCT vs. Other Couples Therapy	Intensive vs. Brief Couples Therapy	Parental Skills & BCT vs. BCT alon
***K*(total N)**	7(486)	3(114)	2(216)	1(20)
Study ID	FALSSTEWART2005 FALSSTEWART2006 LAM2009 OFARRELL1992 SOBELL2000 VEDEL2008 WALITZER2004	FALSSTEWART2005 OFARRELL1992 WALITZER2004	FALSSTEWART2005 ZWEBEN1988	LAM2009
Diagnosis (when reported)	DSM alcohol dependent FALSSTEWART2005 DSM dependent/abuse FALSSTEWART2006 LAM2009 VEDEL2008	DSM alcohol dependent FALSSTEWART2005	DSM alcohol dependent FALSSTEWART2005	DSM dependent/abuse LAM2009
Baseline severity	FALSSTEWART2005 *-Percent days heavy drinking: 56-59% across groups* FALSSTEWART2006 *-Percent days abstinent: 40-44% across groups* LAM2009 *-Percent days abstinent: approx 37%* OFARRELL1992 *-MAST score >7* *-Years of problem drinking: 15.79 years* *-Previous alcohol hospitalisations: 2.09* SOBELL2000 *-ADS score: 12.6* *-Proportion days abstinent: 0.22 approx.* *- Proportion days 1-4 drinks: 0.35 approx.* *- Proportion days 5-9 drinks: 0.32 approx.* *- Proportion days 10+ drinks: 0.12 approx.* *-Mean number of drinks per drinking day: 6 drinks approx.* VEDEL2008 *-62% alcohol dependent* *-50% when drinking drank 7+ units* *-57% drank daily or nearly daily* WALITZER2004 *-Abstinent days per month: 11 days* *-Frequency of drinking >6 drinks per drinking period per month: 5.1* *-ADS score: 8.4* *-85% low dependence; 15% moderate dependence*	FALSSTEWART2005 *-Percent days heavy drinking: 56-59% across groups* OFARRELL1992 *-MAST score >7* *-Years of problem drinking: 15.79 years* *-Previous alcohol hospitalisations: 2.09* WALITZER2004 *-Abstinent days per month: 11 days* *-Frequency of drinking >6 drinks per drinking period per month: 5.1* *-ADS score: 8.4* *-85% low dependence; 15% moderate dependence*	FALSSTEWART2005 *-Percent days heavy drinking: 56-59% across groups* ZWEBEN1988 *-ADS core: 8.4* *-MAST score: approx 20* *-44% heavy drinking in past year* *-36.5% abstinent in the past year*	LAM2009 *-Percent days abstinent: approx 37%*

	Couples Therapy vs. Other Active Intervention	**BCT vs. Other Couples Therapy**	**Intensive vs. Brief Couples Therapy**	**Parental Skills & BCT vs. BCT alone**
Number of sessions	Range: 4-18 sessions	Range: 10-12 sessions	Range: 1-12 sessions	12 sessions

Length of treatment	Range: 4-12 weeks	Range: 10-12 weeks	Range: 1-12 weeks	12 weeks
Length of Follow-up	Range: 2-24 months	Range: 2-24 months	Range: 2-24 months	6 & 12 month
Setting	Outpatient Treatment Centre FALSSTEWART2005 FALSSTEWART2006 LAM2009 OFARRELL1992 VEDEL2008 WALITZER2004 Outpatient Research Unit SOBELL2000	Outpatient Treatment Centre FALSSTEWART2005 OFARRELL1992 WALITZER2004	Outpatient Treatment Centre FALSSTEWART2005 ZWEBEN1988	Outpatient Treatment Centre LAM2009
Treatment Goal	Abstinence FALSSTEWART2006 OFARRELL1992 Drinking Reduction/Moderation SOBELL2000 [30] WALITZER2004 Abstinence OR controlled drinking VEDEL2008[31] Not explicitly stated FALSSTEWART2005 LAM2009	Abstinence OFARRELL1992 Drinking Reduction/ Moderation WALITZER2004 Not explicitly stated FALSSTEWART2005	Abstinence OR Drinking Reduction/Moderation ZWEBEN1988 Not explicitly stated FALSSTEWART2005	Not explicitly stated LAM2009
Country	FALSSTEWART2005 (USA) FALSSTEWART2006 (USA) LAM2009 (USA) OFARRELL1992 (USA) SOBELL2000 (Canada) VEDEL2008 (Netherlands) WALITZER2004 (USA)	FALSSTEWART2005 (USA) OFARRELL1992 (USA) WALITZER2004 (USA)	FALSSTEWART2005 (USA)* ZWEBEN1988 (Canada)	LAM2009 (USA)

6.13.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Couples therapy versus ***other active intervention***

Not significant difference was observed between couples therapy (all types) and other active interventions in maintaining abstinence at post treatment and 2 month follow-up assessment. However, over longer periods, couples therapy was significantly more effective than other therapies in maintaining abstinence and/or light drinking (moderate effect size) when assessed up to 12 month follow-up. This difference was not observed in follow-up periods longer than 12 months. An additional randomised study (MCCRADY2009) could not be included in these analyses as no extractable data was provided. The study reported the BCT was more effective than individual coping skills treatment in maintaining abstinence and reducing heavy drinking days.

[30] Guidelines were stipulated for controlled drinking. Patients could choose a moderation goal unless medical contraindications of drinking require complete abstinence from drinking alcohol.

[31] Guidelines were stipulated for controlled drinking.

Couples therapy was significantly more effective than other active interventions in reducing heavy drinking episodes when assessed up to 12 month follow up. However, there was no difference between couples therapy and other active interventions post-treatment.

The VEDEL2008 study assessed severity of relapse in their sample. The results indicated that other active intervention (namely CBT) was more effective than couples therapy (namely BCT) in reducing occasions in which participants lapsed drank over six drinks on one occasion) or relapsed (drank more than six drinks most days of the week, but no significant difference was observed in the number of participants who relapsed on a regular basis (a few times a month). It must be noted that effect sizes were small and from a single study.

No difference in attrition rates was observed between groups post-treatment and at 3 month follow-up. Couples therapy had less attrition than other therapies at 6 month follow up (large effect size), and other therapies had less attrition than couples therapy at 12 month follow-up (large effect size).

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 32.

BCT versus other couples therapy

No significant difference was observed between BCT and other forms of couples therapy in maintaining abstinence when assessed post-treatment and up to 24 month follow-up. Similarly no difference between these groups was observed in reducing heavy drinking and attrition rates post-treatment and up to 12 month follow-up.

The quality of this evidence is *moderate* and further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 33.

Intensive versus standard couples therapy

At one month follow up, brief couples therapy was more effective than more intensive couples therapy in maintaining abstinence (moderate effect size). However, this difference was not maintained up to 18 month follow-up. Furthermore, no significant benefit of more intensive couples therapy over brief couples therapy in reducing heavy drinking was observed up to 18 month follow-up. Those who received more intensive couples therapy were more likely to be retained for follow-up assessment at 12 months than brief couples therapy (small effect size).

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 34.

Parental skills & BCT versus ***BCT alone***

The addition of parental skills training to BCT did not significant improve abstinence rates both post-treatment and up to 12 month follow-up.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect, An evidence summary of the results of the meta-analyses can be seen in Table 35.

Table 61. Couples Therapy vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method
Abstinence		
Abstinence (% or Proportion) Post Treatment	214	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) Up to 6 month Follow Up		
% Days Abstinent at 2 month follow-up	34	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent at 3 month follow-up	138	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent/Light (no alcohol or 1-3 drinks) at 3 Month Follow Up	63	Std. Mean Difference (IV, Random, 95% CI)
% days Abstinent at 6 month follow-up	202	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent/Light (no alcohol or 1-3 drinks) at 6 Month Follow Up	63	Std. Mean Difference (IV, Random, 95% CI)
Abstinence % or Proportion) 7 - 12 Month Follow Up		
% Days Abstinent at 9 month follow-up	138	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent/Light (no alcohol or 1-3 drinks) at 9 Month Follow Up	61	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent at 12 month follow-up	245	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent/Light (no alcohol or 1-3 drinks) at 12 Month Follow Up	61	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) >12 month Follow Up		
at 18 months	34	Std. Mean Difference (IV, Random, 95% CI)
at 24 months	34	Std. Mean Difference (IV, Random, 95% CI)
Lapse or Relapse		
Relapse (>6 units most days of the week) Post Treatment	48	Risk Ratio (M-H, Random, 95% CI)
Regular Relapse (>6 units a few times a month) Post Treatment	48	Risk Ratio (M-H, Random, 95% CI)
Severe lapse (>6 units on one occasion) Post Treatment	48	Risk Ratio (M-H, Random, 95% CI)
Rates of Consumption		
Rates of Consumption Post Treatment		
% Days Heavy Drinking Post Treatment	152	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption Up to 6 Month Follow Up		
% Days Heavy Drinking(>6 drinks per day) at 3 Month Follow Up	215	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>6 drinks per day) at 6 Month Follow Up	215	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption 7 - 12 Month Follow Up		
Days Light Drinking (Proportion) at 12 Month Follow Up	43	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>6 drinks per day) at 9 Month Follow Up	213	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>6 drinks per day) at 12 Month Follow Up	213	Std. Mean Difference (IV, Random, 95% CI)
Days Drinking 5-9 Drinks (Proportion) at 12 month Follow Up	43	Std. Mean Difference (IV, Random, 95% CI)
Days Drinking >= 10 drinks(proportion) at 12 Month Follow Up	43	Std. Mean Difference (IV, Random, 95% CI)
Amount of Alcohol Consumed		
Amount of Alcohol Consumed Post Treatment		
Units Per Week	48	Std. Mean Difference (IV, Random, 95% CI)
Amount of Alcohol Consumed Up to 6 month Follow Up		
Units Per Week at 6 month Follow Up	45	Std. Mean Difference (IV, Random, 95% CI)
Amount of Alcohol Consumed at 7- 12 Month Follow Up		
Mean no. drinks per drinking day at 12 month Follow Up	43	Std. Mean Difference (IV, Random, 95% CI)
Attrition (Drop-Out)		
Attrition (Drop-out) Post Treatment	313	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-out) up to 6 Month Follow Up		
at 3 month Follow Up	64	Risk Ratio (M-H, Random, 95% CI)
at 6 month Follow Up	111	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-out) 7-12 month Follow Up		
at 9 month Follow Up	63	Risk Ratio (M-H, Random, 95% CI)
at 12 month Follow Up	242	Risk Ratio (M-H, Random, 95% CI)

Table 62. Behavioural Couples Therapy (BCT) vs. Other Couples Therapy Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method
Abstinence		
Abstinence (% or Proportion) Post Treatment	22	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) Up to 6 month Follow Up		
at 2 month Follow Up	22	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent/Light (no alcohol or 1-3 drinks) at 3 month Follow Up	41	Std. Mean Difference (IV, Random, 95% CI)
at 6 month Follow Up	22	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent/Light (no alcohol or 1-3 drinks) at 6 month Follow Up	41	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) 7 - 12 Month Follow Up		
% Days Abstinent or Light (no alcohol or 1-3 drinks) at 9 month Follow Up	41	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent at 12 month Follow Up	22	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent or Light (no alcohol or 1-3 drinks) at 12 month Follow Up	41	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) >12 month Follow Up		
at 18 months Follow Up	22	Std. Mean Difference (IV, Random, 95% CI)
at 24 month Follow Up	22	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption		
Rates of Consumption Post Treatment		
% Days Heavy Drinking	50	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption Up to 6 Month Follow Up		
% Days Heavy Drinking (>6 drinks per day) at 3 month Follow Up	91	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>6 drinks per day) at 6 month Follow Up	91	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption 7 - 12 Month Follow Up		
% Days Heavy Drinking (>6 drinks per day) at 9 month Follow Up	91	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>6 drinks per day) at 12 month Follow Up	91	Std. Mean Difference (IV, Random, 95% CI)
Attrition (Drop-Out)		
Attrition (Drop-Out) Post Treatment	22	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-Out) up to 6 Month Follow Up		
at 3 month follow-up	42	Risk Ratio (M-H, Random, 95% CI)
at 6 month Follow Up	41	Risk Ratio (M-H, Random, 95% CI)
at 9 month Follow Up	42	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-Out) 7 - 12 Month Follow Up	41	Risk Ratio (M-H, Random, 95% CI)
at 12 month Follow Up	41	Risk Ratio (M-H, Random, 95% CI)

Table 63. Intensive Couples Therapy vs. Brief Couples Therapy Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method
Abstinence		
Abstinence (% or Proportion) Up to 6 month Follow Up		
at 1 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
at 2 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
at 6 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) 7 - 12 Month Follow Up		
at 12 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (% or Proportion) >12 month Follow Up		
at 18 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption		
Rates of Consumption Post Treatment		
% Days Heavy Drinking	50	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption Up to 6 Month Follow Up		
% Days Heavy Drinking (> 6 drinks per day) at 1 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (> 6 drinks per day) at 2 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (> 6 drinks per day) at 3 month Follow Up	50	Std. Mean Difference (IV, Random, 95% CI)

% Days Heavy Drinking (> =5 drinks per day) at 6 month Follow Up	166	Std. Mean Difference (IV, Random, 95% CI)
% Moderate Drinking Days (1-4 drinks per day) at 1 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
% Moderate Drinking Days (1-4 drinks per day) at 2 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
% Moderate Drinking Days (1-4 drinks per day) at 6 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption 7 - 12 Month Follow Up		
% Moderate Drinking Days (1-4 drinks per day) at 12 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (> 6 drinks per day) at 9 month Follow Up	50	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>=5 drinks per day) at 12 month Follow Up	166	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption > 12 month Follow Up		
% Moderate Drinking Days (1-4 drinks per day) at 18 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
% Days Heavy Drinking (>=5 drinks per day) at 18 month Follow Up	116	Std. Mean Difference (IV, Random, 95% CI)
Attrition (Drop-Out)		
Attrition (Drop-Out) Post Treatment	218	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-Out) > 12 month Follow Up at 1-18 month Follow Up	163	Risk Ratio (M-H, Random, 95% CI)

Table 64. Parental Skills + BCT vs. BCT alone Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method
Abstinence		
% Days Abstinent Post Treatment	20	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent at 6 Month Follow Up	20	Std. Mean Difference (IV, Random, 95% CI)
% Days Abstinent at 12 month follow up	20	Std. Mean Difference (IV, Random, 95% CI)

6.14 Counselling

6.14.1 Definition

The British Association for Counselling and Psychotherapy defines counselling as 'a systematic process which gives individuals an opportunity to explore, discover and clarify ways of living more resourcefully, with a greater sense of well-being' (British Association of Counselling, 1992). This definition, which has been used in other NICE guidelines, was adopted for this review but in the included studies counselling for alcohol treatment was not often well-defined or manual-based making decisions about inclusion difficult, where there was uncertainty this was resolved in discussion with the GDG.

6.14.2 Clinical review protocol (Counselling)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 299).

Table 65. Clinical review protocol for the review of Counselling.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Counselling
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.14.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of counselling in the treatment of alcohol dependence or harmful alcohol use. See Table 37 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Five trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=630 participants. All five studies were published in peer-reviewed journals between 1986 and 2003. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Counselling studies were mainly excluded for not being randomised trials. When studies did meet basic methodological inclusion criteria, the main reason for exclusion were that treatment was opportunistic as opposed to planned, the study was not directly relevant to the clinical questions, or no relevant alcohol-focused outcomes were available. A list of excluded studies can be found in Appendix 16d.

Counselling versus control

Of the five included trials, there was only one involving a comparison of counselling versus control which met criteria for inclusion. SELLMAN2001 assessed counselling (non-directive reflective listening) versus control (no further treatment – feedback only).

Counselling versus other active intervention

All five included trials assessed counselling versus another active intervention and met criteria for inclusion. ERIKSEN1986 assessed counselling (group) versus social skills training (coping skills), JOHN2003 assessed counselling (individual) versus multi-modal standard intervention (see Appendix 16d for more information), LITT2003 assessed counselling (group) versus coping skills, O'FARRELL1992 assessed counselling (individual) versus both interactional couples therapy and

behavioural marital therapy, and SELLMAN2001 assessed counselling (non-directive reflective listening) versus MET. The included studies were conducted between 1986 and 2003.

Table 66. Summary of study characteristics for Counselling

	Counselling vs. Control	Counselling vs. Other Active Intervention
***K*(total N)**	1(80)	5(590)
Study ID	SELLMAN2001	ERIKSEN1986 JOHN2003 LITT2003 O'FARRELL1992 SELLMAN2001
Diagnosis	DSM alcohol dependent SELLMAN2001	ICD-10 alcohol dependent JOHN2003 DSM alcohol dependent SELLMAN2001 DSM alcohol dependent/abuse LITT2003
Baseline severity	SELLMAN2001 *-Unequivocal heavy drinking 6+ times in 6 month follow-up period: 90.2%*	ERIKSEN1986 *-Previous alcoholism inpatient status: 66.7%* LITT2003 *-Drinking days 6 months prior to intake: 72%* O'FARRELL1992 *-MAST Score: >7* SELLMAN2001 *-Unequivocal heavy drinking 6+ times in 6 month follow-up period: 90.2%*
Number of sessions	4 sessions	Range: 8-26
Length of treatment	6 weeks	Range: 3-26 weeks
Length of FU (only including papers reporting FU Measures)	6 month & 5 year	Range: 2 months – 5 years
Setting	Outpatient Treatment Centre SELLMAN2001	Inpatient ERIKSEN1986 JOHN2003 Outpatient Treatment Centre O'FARRELL1992 SELLMAN2001 Outpatient Research Unit LITT2003
Treatment Goal	Not explicitly Stated SELLMAN2001	Abstinence JOHN2003 O'FARRELL1992 Drinking Reduction/Moderation ERIKSEN1986 Not explicitly stated LITT2003 SELLMAN2001
Country	SELLMAN2001 (New Zealand)	ERIKSEN1986 (Norway) JOHN2003 (Germany) LITT2003 (USA) O'FARRELL1992 (USA) SELLMAN2001 (New Zealand)

6.14.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Counselling versus ***Control***

Based on the SELLMAN2001 study, no significant difference was observed between treatment groups, hence, the clinical evidence does not support the benefits of counselling over control in maintaining abstinence or reducing heavy drinking.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 38.

Counselling versus other active intervention

In maintaining abstinence, no significant difference was observed between counselling and other therapies when assessed up to 6 month follow-up. However, bar the 6 month follow-up, these results are based on a single study (O'FARRELL1992) whereas in the analyses assessing couples therapies versus other active therapies, more studies were included in the analyses for this outcome. Other therapies (namely couples therapies and coping skills) showed significant benefits over counselling in maintaining abstinence at longer follow-up periods of up to 18 months.

Overall, no significant difference was observed between counselling and other therapies up to 18 month follow-up in time to first drink (lapse), time to first heavy drink (relapse) and reducing heavy drinking episodes. These analyses were based on data from a single study (LITT2003). However, other therapies (coping skills) were more effective than counselling in reducing amount of alcohol consumed when assessed at 12 month follow-up. Again, this result was based on a single study (ERIKSEN1986) limiting the ability to generalise the findings.

Lastly, no significant difference was observed between counselling and other therapies in attrition rates.

The quality of this evidence is moderate therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 39.

Table 67. Counselling vs. Control Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Rates of Consumption			
Rates of Consumption up to 6 month follow up			
Exceeded National Guidelines at least once (at 6 months)	80	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.83, 1.38]
Exceeded National Guideline >=6 times (at 6 months)	80	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.83, 1.38]
Drank >=10 standard drinks at least once (at 6 months)	80	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.77, 1.22]
Drank >=10 standard drinks >= 6 times (at 6 months)	80	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.69, 1.34]
Rates of Consumption >12 month follow-up			
Exceeded National Guidelines at least once (at 5 years)	50	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.62, 1.45]
Exceeded National Guidelines >= 6 times (at 5 years)	50	Risk Ratio (M-H, Random, 95% CI)	1.09 [0.62, 1.89]
Drank >=10 standard drinks at least once (at 5 years)	50	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.38, 1.41]
Drank >=10 standard drinks >=6 times (at 5 years)	50	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.22, 1.73]
Lapse or Relapse			
Lapse up to 6 month Follow Up			
Broke Abstinence (lapse) at 6 months	80	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.85, 1.11]
Lapse >12 month Follow Up			
Broke Abstinence (lapse) at 5 years	50	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.73, 1.38]
Attrition (Drop-Out)			
Attrition (Drop-out) Post Treatment	80	Risk Ratio (M-H, Random, 95% CI)	Not estimable
Attrition (Drop-out) >12 month Follow Up			
at 5 year follow up	80	Risk Ratio (M-H, Random, 95% CI)	1.73 [0.95, 3.15]

Table 68. Counselling vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method
Abstinence		
Abstinence (Percentage) Post Treatment	34	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (Percentage or Proportion) Up to 6 Months		
% days abstinent at 2 month Follow Up	34	Std. Mean Difference (IV, Random, 95% CI)
% days abstinent at 3 month Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
% days abstinent at 6 month Follow Up	162	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (Percentage or Proportion) at 7-12 Month Follow Up		
Sober Days at 12 month follow up	23	Std. Mean Difference (IV, Random, 95% CI)
% days abstinent at 9 months Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
% days abstinent at 12 month Follow Up	162	Std. Mean Difference (IV, Random, 95% CI)
Abstinence (Percentage or Proportion) >12 Month Follow Up		
% days abstinent at 15 month Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
% days abstinent at 18 month Follow Up	162	Std. Mean Difference (IV, Random, 95% CI)
% days abstinent at 24 month Follow Up	34	Std. Mean Difference (IV, Random, 95% CI)
Lapse or Relapse		
Lapse up to 6 month Follow Up		
Broke Abstinence (lapse) at 6 month Follow Up	404	Risk Ratio (M-H, Random, 95% CI)
Lapsed - 7-12 month follow-up		
at 12 month follow-up	322	Risk Ratio (M-H, Random, 95% CI)
Lapse >12 month Follow Up		
Broke Abstinence (lapse) at 5 year Follow Up	48	Risk Ratio (M-H, Random, 95% CI)
Rates of Consumption		
Rates of Consumption Up to 6 Month Follow Up		
Proportion Days Heavy Drinking (>= 6 men, 4 women) at 3 months Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Proportion Days Heavy Drinking (>= 6 men, 4 women) at 6 months Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption 7-12 Month Follow Up		
Proportion Days Heavy Drinking (>= 6 men, 4 women) at 9 month	128	Std. Mean Difference (IV, Random, 95% CI)

Follow Up		
Proportion Days Heavy Drinking (>= 6 men, 4 women) at 12 months Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption >12 Month Follow Up		
Proportion Days Heavy Drinking (>= 6 men, 4 women) at 15 months Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Proportion Days Heavy Drinking (>= 6 men, 4 women) at 18 months Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Rates of Consumption up to 6 Month Follow Up		
Exceeded National Guidelines at least once (at 6 months)	82	Risk Ratio (M-H, Random, 95% CI)
Exceeded National Guideline >=6 times (at 6 months)	82	Risk Ratio (M-H, Random, 95% CI)
Drank >=10 standard drinks at least once (at 6 months)	82	Risk Ratio (M-H, Random, 95% CI)
Drank >=10 standard drinks >= 6 times (at 6 months)	82	Risk Ratio (M-H, Random, 95% CI)
Rates of Consumption >12 Months Follow up		
Exceeded National Guidelines at least once (at 5 years)	48	Risk Ratio (M-H, Random, 95% CI)
Exceeded National Guidelines >= 6 times (at 5 years)	48	Risk Ratio (M-H, Random, 95% CI)
Drank >=10 standard drinks at least once (at 5 years)	48	Risk Ratio (M-H, Random, 95% CI)
Drank >=10 standard drinks >=6 times (at 5 years)	48	Risk Ratio (M-H, Random, 95% CI)
Amount of Alcohol Consumed		
Amount of Alcohol Consumed at 7-12 month Follow Up		
cl pure alcohol at 12 month follow up	23	Std. Mean Difference (IV, Random, 95% CI)
Time to First Drink Assessed at 18 Month Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Time to First Heavy Drink Assessed at 18 Month Follow Up	128	Std. Mean Difference (IV, Random, 95% CI)
Attrition (Drop-Out)		
Attrition (Drop-Out) Post Treatment	128	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-Out) up to 6 months follow-up		
at 3-6 month follow-up	322	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-out) 7-12 Month Follow Up		
at 12 month follow up	247	Risk Ratio (M-H, Random, 95% CI)
Attrition (Drop-out) >12 month Follow Up		
at 5 year follow up	82	Risk Ratio (M-H, Random, 95% CI)

6.15 Psychodynamic Therapy

6.15.1 Definition

Short-term psychodynamic therapy is a derived from a psychodynamic/ psychoanalytic model in which: a) therapist and patient explore and gain insight into conflicts and how these are represented in current situations and relationships, including the therapy relationship; b) service users are given an opportunity to explore feelings and conscious and unconscious conflicts originating in the past, with the technical focus on interpreting and working through conflicts; c) therapy is non-directive and service users are not taught specific skills such as thought monitoring, re-evaluation or problem solving. Treatment typically consists of 16–30 sessions (Leichsenring et al., 2004) but there are interventions which offer more or less than this range.

6.15.2 Clinical review protocol (Psychodynamic Therapy)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 69. Clinical review protocol for the review of Psychodynamic Therapy.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Psychodynamic Therapy
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.15.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of psychodynamic therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 41 for a summary of the study characteristics.

One trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=49 participants. The study was published in peer-reviewed journals in 1998. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were further excluded because they did not meet methodological criteria (see Chapter 3). When studies did meet basic methodological inclusion criteria, the main reasons for exclusion were that the study was not directly relevant to the clinical questions, or no relevant alcohol-focused outcomes were available. A list of excluded studies can be found in Appendix 16d.

Psychodynamic therapy versus other active intervention

The single trial which was suitable for inclusion was SANDAHL1998 and it investigated group-based time-limited group psychotherapy (or a short-term psychodynamic therapy as described above) versus another active intervention which in this case was relapse prevention.

Table 70. Summary of study characteristics for Psychodynamic Therapy

	Psychodynamic Therapy vs. Other Active Intervention
***K*(total N)**	1(49)
Study ID	SANDAHL1998
Diagnosis (when available)	DSM III-R alcohol dependence
Baseline severity	-Duration of alcohol abuse: 11 years -Reported morning drinking:75.5%
Number of sessions	15 sessions
Length of treatment	15 weeks
Length of Follow-up	15 month
Setting	Outpatient Treatment Centre
Treatment Goal	Drinking Reduction/Moderation
Country	Sweden

6.15.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Psychodynamic therapy versus other active intervention

At 15 month follow-up, psychodynamic therapy was significantly more effective than other therapies (in this case cognitive behavioural relapse prevention) in maintaining abstinence, although the effect size was moderate. However, no significant difference was observed between psychodynamic therapy and other therapies in reducing the quantity of alcohol consumed, heavy drinking rate or attrition. It must be noted that this analysis was based on a single study.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 42.

Table 71. Psychodynamic Therapy vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Days Abstinent at 15 month Follow-up	44	Std. Mean Difference (IV, Random, 95% CI)	-0.64 [-1.24, -0.03]
Rates of Consumption			
Days > 80g abs.alc (Heavy Drinking) at 15 month Follow Up	44	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.65, 0.53]
Amount of Alcohol Consumed			
Grams abs.alc/drinking day at 15 Month Follow-up	44	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.53, 0.66]
Attrition (Drop-Out)			
at 15 month Follow Up	49	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.12, 3.50]

6.16 Multi-Modal Treatment

6.16.1 Definition

Multi-modal treatment for alcohol misuse involves a combination of a number of interventions which have been developed and evaluated as standalone interventions for alcohol misuse. Components of a multi-modal treatment could include motivational aspects (such as MET), TSF, AA or self-help group participation, group counselling, CBT based relapse-prevention training and psychoeducational sessions. The intention is that by combining a number of effective interventions the combined treatment will be greater than any one individual treatment.

6.16.2 Clinical review protocol (Multi-Modal Treatment)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 72. Clinical review protocol for the review of Multi-Modal Treatment.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Multi-Modal Treatment
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.16.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of multi-modal therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 44 for a summary of the study characteristics.

Two trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=427 participants. Both studies were published in peer-reviewed journals between 2002 and 2003. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was that no relevant alcohol-focused outcomes were available. A list of excluded studies can be found in Appendix 16d.

Multi-Modal Treatment versus other active intervention

Both included trials which met criteria for inclusion assessed multi-modal treatment versus another active intervention. DAVIS2002 assessed standard multi-modal outpatient treatment versus psychoeducational intervention. Standard multi-modal treatment included a three week orientation period which consisted of six group therapy sessions, three alcohol education and three leisure education films, three community meetings, and a minimum of six AA meetings. After orientation, participants were assigned to a permanent therapist for a mixture of individual and group therapy sessions tailored to the needs of the participant. JOHN2003 assessed multi-modal standard inpatient and outpatient treatment versus individual counselling. Standard treatment was based on the principles of motivational interviewing, relapse prevention, and psychoeducational films with a focus to support the motivation to seek help for substance-use problems.

Table 73. Summary of study characteristics for Multi-Modal Treatment

	Multi-Modal Treatment vs. Other Active Intervention
***K*(total N)**	2(427)
Study ID	DAVIS2002 JOHN2003
Diagnosis (when available)	Treatment-seeking alcohol abuse or dependent DAVIS2002 ICD-10 alcohol dependent JOHN2003
Baseline severity	DAVIS2002 *-Days drinking in last 6 months: approx 110 days*
Number of sessions	Variable (see description of treatment modalities)
Length of treatment	Variable from 14 days inpatient (JOHN2003) to 6 months inpatient and outpatient (DAVIS2002)
Length of Follow-up	Range: 6 - 12 months
Setting	Outpatient Treatment Centre DAVIS2002 Inpatient JOHN2003
Treatment Goal	Abstinence JOHN2003 Drinking Reduction/Moderation DAVIS2002
Country	DAVIS2002 (USA) JOHN2003 (Germany)

6.16.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Multi-Modal versus other active intervention

A small effect was observed favouring other therapies (i.e. psychoeducational) over multi-modal treatment in maintaining abstinence when assessed post-treatment. In

additional other therapies (i.e. counselling) were significantly better than multi-modal treatment in reducing the number of participants who had lapsed (small effect size). However, this was not the case at 12 months follow-up as no difference between groups was observed. Furthermore, no difference was observed between multi-modal treatment and other therapies in reducing the number of days drinking, the quantity of alcohol consumed, and attrition up to 12 month follow-up.

The quality of this evidence is *low* therefore further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate. An evidence summary of the results of the meta-analyses can be seen in Table 45.

Table 74. Multimodal Intervention vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Length of Sobriety (in months) Post Treatment	77	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.02, 0.93]
Lapse or Relapse			
Lapsed Post Treatment	84	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.60, 1.03]
Lapsed up to 6 month follow-up at 6 months	322	Risk Ratio (M-H, Random, 95% CI)	1.23 [1.04, 1.45]
Lapsed - 7-12 month follow-up at 12 month follow-up	322	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.81, 1.05]
Rates of Consumption			
Days Drinking Post Treatment	80	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.85, 0.04]
Amount of Alcohol Consumed			
oz./day Post Treatment	75	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.71, 0.21]
Attrition (Drop-Out)			
Attrition (Drop-Out) Post Treatment	89	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.43, 2.57]
Attrition (Drop-Out) up to 6 months follow-up at 6 month follow-up	322	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.74, 1.42]
Attrition (Drop-out) at 7-12 month follow-up at 12 month follow-up	223	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.67, 1.09]

6.17 Self-help based treatment

6.17.1 Definition

A self-help intervention is where a healthcare professional (or para-professional) would facilitate the use of the self-help material by introducing, monitoring and reviewing the outcome of such treatment. The intervention is limited in nature, usually no more than three to five sessions some of which may be delivered by telephone. Self-administered intervention are designed to modify drinking behaviour and makes use of a range of books, web pages, CD-ROMs or a self-help manual that is based on an evidence-based intervention and designed specifically for the purpose. An example is Guided Self Change (GSC) (Sobell & Sobell, 1993). This treatment is manual-based and uses the principles of cognitive behavioural therapy and motivational enhancement therapy. The patient has an initial assessment followed by four treatment sessions and two follow-up telephone calls.

6.17.2 Clinical review protocol (Self-help Based Treatment)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 75. Clinical review protocol for the review of Self-Help Based Treatment.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Self-Help Based Treatment
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.17.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of self-help based treatment in the treatment of alcohol dependence or harmful alcohol use. See Table 47 for a summary of the study characteristics.

One trial relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=93 participants. The included study was published in a peer-reviewed journal in 2002. A number of studies identified in the search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). A particular problem for self-helped based treatments is that they usually fall under the grouping of 'brief interventions' Therefore, the main reasons for exclusions were the population assessed were hazardous drinkers (outside the scope of this guideline), the population were not treatment seeking, or no relevant alcohol-focused outcomes were available. A list of excluded studies can be found in Appendix 16d.

Guided self-help based treatment (guided) versus non-guided self-help based treatment

The single trial include in this analyses involved a comparison of guided self-help based treatment (guided) versus non-guided self-help based treatment. ANDREASSON2002 assessed guided self change versus self-help manual and advice only (non-guided).

Table 76. Summary of study characteristics for Self-Help Based Treatment

	Self-Help Based Treatment (guided) vs. Self-Help Based Treatment (non-guided)
***K*(total N)**	1(93)
Study ID	ANDREASSON2002
Diagnosis (when available)	SADD score of 12.1 indicating a medium level of alcohol dependence
Baseline severity	-Number of drinks per week: 24.3 drinks -Number of drinks per drinking day: 5.7
Number of sessions	Guided Self-Help *Assessment = 1 session* *Treatment = 4 sessions* *Follow-up = 2 telephone calls* Non-Guided Self-Help *Assessment = 1 session* *Treatment = 1 session*
Length of treatment	N/A
Length of Follow-up	9 & 23 month
Setting	Outpatient Treatment Centre
Treatment Goal	Not explicitly Stated
Country	Sweden

6.17.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Guided self-help based treatment (guided) versus non-guided self-help based treatment

Guided self-help was significantly more effective than non-guided self-help in reducing the quantity of drinks consumed per week when assessed at 9 month follow-up. However, no significant difference was observed between group for the same variable at 23 month follow-up as we as the number of drinks per drinking day (at 9 and 23 month follow-up) or attrition at 23 month follow-up.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 48.

Table 77. Comparing Different Formats of Self-Help Based Treatment Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Es
Amount of Alcohol Consumed			
Amount of Alcohol Consumed at 7-12 Month Follow Up			
Number Standard Drinks Per week at 9 month Follow Up	59	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-1.0
Number of Drinks per Drinking Day at 9 month Follow-up	59	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.7
Amount of Alcohol consumed >12 Month Follow Up			
Number of Standard Drinks per Week at 23 month Follow-up	59	Std. Mean Difference (IV, Random, 95% CI)	-0.45 [-0.9
Number of Drinks per Drinking Day at 23 month Follow-up	59	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.6
Attrition (Drop-Out)			
Attrition at 23 Month Follow Up	93	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.5

6.18 Psychoeducational Interventions

6.18.1 Definition

A psychoeducational intervention involves an interaction between an information provider and service user, which has the primary aim of offering information about the condition and providing support and management strategies. Psychoeducational intervention for alcohol misuse involves the use of education videos, literature and lectures which highlight the health and lifestyle risks of excessive alcohol consumption. It is not usually used as a formal method of treatment, but an adjunct to conventional treatment methods. Psychoeducational attention control treatment (PACT) is a form of manual-based psychoeducational therapy developed by Fals-Stewart & Klostermann (2004) and used in some alcohol treatment trials.

6.18.2 Clinical review protocol (Psychoeducational Interventions)

Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3 (further information about the search for health economic evidence can be found in Section 6.21).

Table 78. Clinical review protocol for the review of Psychoeducational Intervention.

Electronic databases	COCHRANE, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm)
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Psychoeducational Intervention
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.18.3 Studies considered for review

The review team conducted a systematic review of RCTs that assessed the beneficial or detrimental effects of behavioural therapies in the treatment of alcohol dependence or harmful alcohol use. See Table 50 for a summary of the study characteristics. It should be noted that some trials included in analyses were three- or four-arm trials. In order to avoid double-counting, the number of participants in treatment conditions used in more than one comparison was divided (by half in a three-arm trial, and by three in a four-arm trial).

Five trials relating to clinical evidence met the eligibility criteria set by the GDG, providing data on n=1312 participants. All five studies were published in peer-reviewed journals between 2001 and 2006. A number of studies identified in the

search were initially excluded because they were not relevant to this guideline. Studies were excluded because they did not meet methodological criteria (see methods Chapter 3). When studies did meet basic methodological inclusion criteria, the main reason for exclusion was not meeting drinking quantity/diagnosis criteria, i.e. participants were not drinking enough to be categorised as harmful or dependent drinkers or less than 80% of the sample meet criteria for alcohol dependence or harmful alcohol use. A list of excluded studies can be found in Appendix 16d.

Psychoeducational intervention versus other active intervention

All five included trials assessed psychoeducational therapy versus another active intervention inclusion. CONNORS2001 was complex in design and investigated psychoeducational therapy plus alcohol-focused coping skills versus life skills plus alcohol-focused coping skills. Additionally, the study investigated the difference between low and high intensity treatment of these conditions. The results of the thirty month follow-up were obtained from Walitzer & Connors (2007). DAVIS2002 assessed psychoeducational therapy versus standard multi-modal treatment. FALSSTEWART2005 investigated psychoeducational therapy (used as an attentional control) versus behavioural couples therapy (plus group counselling), brief relationship therapy (plus group counselling) and individually based TSF (plus group counselling). FALSSTEWART2006 investigated psychoeducational therapy (as an attentional control) versus behavioural couples therapy (plus individually-based TSF) as well as individually-based twelve-step facilitation alone. SOBELL2002 investigated psychoeducational (bibliotherapy/drinking guidelines) versus motivational enhancement/personalised feedback.

Table 79. Summary of study characteristics for Psychoeducational Intervention

	Psychoeducational vs. Other Active Intervention
***K*(total N)**	5(1312)
Study ID	CONNORS2001 DAVIS2002 FALSSTEWART2005 FALSSTEWART2006 SOBELL2002
Diagnosis (when available)	DSM alcohol dependent CONNORS2001 FALSSTEWART2005 FALSSTEWART2006 DSM alcohol dependent/abuse DAVIS2002
Baseline severity	CONNORS2001 *-Percent of sample severe dependence: 8.3%* *-Percent of sample moderate dependence: 66%* *-Percent of sample mild dependence: 18.1%* *-Average monthly abstinent days: 10.1 days* *-Average monthly light days: 6.1 days* *-Average monthly moderate days: 8 days* *-Average monthly heavy days: 5.7 days* DAVIS2002 *-Days drinking over 6 months: 110 days* FALSSTEWART2005 *-Percent day heavy drinking: 56-59% across treatment groups* FALSSTEWART2006 *-Percent days abstinent: 40-44% across treatment groups* SOBELL2002 *-Drinking days per week: 5.5 days*

	-Drinks per drinking day: 5 drinks
Number of sessions	Range: 1-26 sessions
Length of treatment	Range: 1-26 weeks
Length of Follow-up	Range: 3-18 months
Setting	Outpatient Treatment Centre DAVIS2002 FALSSTEWART2005 FALSSTEWART2006 Outpatient Clinical Research Unit CONNORS2001 Community Level Mail Intervention SOBELL2002
Treatment Goal	Abstinence FALSSTEWART2006 Drinking Reduction/Moderation CONNORS2001 DAVIS2002 Not explicitly Stated FALSSTEWART2005 SOBELL2002
Country	All USA

6.18.4 Evidence summary

The GRADE profiles and associated forest plots for the comparisons can be found in Appendix 18c and 17c respectively.

Psychoeducational versus other active intervention

The clinical findings for this comparison are mixed whether in favour of other active therapies over a psychoeducational intervention or finding no clinically significant difference between psychoeducational and other therapies. Other therapies were significant better than psychoeducational therapy in increasing length of sobriety (post treatment), and the percentage of abstinent/light drink days at 6 and 12 month follow up.

No significant difference was observed been a psychoeducational intervention and other active therapies in attrition rates and other drinking related variables.

The quality of this evidence is *moderate* therefore further research is likely to have an important impact on our confidence in the estimate of the effect. An evidence summary of the results of the meta-analyses can be seen in Table 51.

Table 80. Psychoeducational Intervention vs. Other Intervention Evidence Summary

Outcome or Subgroup	Number of Participants	Statistical Method	Effect Estimate
Abstinence			
Length of Sobriety (months) Post Treatment	77	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.02, 0.93]
Abstinence Post Treatment			
% Days Abstinent Post Treatment	138	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.32, 0.38]
Abstinence up to 6 month follow up			
at 3 month follow up	138	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.26, 0.50]
at 6 month follow up	138	Std. Mean Difference (IV, Random, 95% CI)	0.30 [-0.23, 0.84]
Abstinence 7-12 month follow up			
at 9 month follow up	138	Std. Mean Difference (IV, Random, 95% CI)	0.28 [-0.35, 0.92]
at 12 month follow up	138	Std. Mean Difference (IV, Random, 95% CI)	0.26 [-0.43, 0.96]
Abstinent/Light (1-3 standard drinks) up to 6 month follow up			
at 6 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	0.94 [0.40, 1.48]
Abstinent/light (1-3 standard drinks) 7-12 month follow up			
at 12 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	0.84 [0.27, 1.40]
Abstinent/Light (1-3 standard drinks) >12 month follow up			
at 18 month follow up	61	Std. Mean Difference (IV, Random, 95% CI)	0.74 [0.21, 1.26]
Number lapsed (non-abstinent) Post Treatment			
at 6 month follow up	84	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.97, 1.66]
Rates of Consumption			
Rate of alcohol consumption Post Treatment	179	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.11, 0.53]
% days heavy drinking at post-treatment	99	Std. Mean Difference (IV, Random, 95% CI)	-0.00 [-0.46, 0.46]
Days Drinking (over last 6 months) Post Treatment	80	Std. Mean Difference (IV, Random, 95% CI)	0.41 [-0.04, 0.85]
Rate of alcohol consumption up to 6 month follow-up			
% days heavy drinking at 3 months	99	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.27, 0.65]
% days heavy drinking at 6 months	99	Std. Mean Difference (IV, Random, 95% CI)	0.37 [-0.10, 0.83]
Rate of alcohol consumption - 7-12 month follow-up			
days drinking per week at 12 month follow-up	657	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.15, 0.15]
days drinking five or more drinks at 12 month follow-up	657	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.08, 0.23]

% days heavy drinking at 9 months	99	Std. Mean Difference (IV, Random, 95% CI)	0.38 [-0.09, 0.84]
% days heavy drinking at 12 months	99	Std. Mean Difference (IV, Random, 95% CI)	0.50 [-0.04, 1.04]
Amount of Alcohol Consumed			
Amount of Alcohol Consumed Post Treatment			
oz./day	75	Std. Mean Difference (IV, Random, 95% CI)	0.25 [-0.21, 0.71]
Amount of alcohol consumed 7-12 month follow up			
drinks per drinking day at 12 month follow-up	657	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.15, 0.15]
drinks per week at 12 month follow-up	657	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.14, 0.16]
Attrition (drop-Out)			
Attrition (drop-out) Post Treatment	227	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.46, 1.87]
Attrition up to 6 month follow up			
at 6 months	144	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.32, 3.19]
Attrition (drop-out) 7-12 month follow up			
at 12 month follow up	1082	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.64, 1.07]
Attrition (drop-out) >12 month follow-up			
at 18 months	130	Risk Ratio (M-H, Random, 95% CI)	0.23 [0.01, 4.67]

6.19 Mindfulness Meditation

6.19.1 Definition

Mindfulness meditation is rooted in the principles of Buddhism and is characterised by having a nonjudgmental approach to experiences that result in the practitioner acting reflectively rather than impulsively on these experiences (Chiesa, 2010). Mindfulness mediation has a goal off developing a nonjudgmental attitude and relationship to thoughts, feelings and actions as they experienced by the practitioner and not necessarily to change the content of thoughts as in CBT for example (Teasdale *et al*., 1995).

Mindfulness-based meditation has been suggested as a method of improving physical and mental health (for a review see Allen *et al*. 2006). However, the quality of this research is generally poor, not focused on alcohol as the substance of abuse, and few in number.

6.19.2 Clinical review protocol

In the current review, the role of meditation in maintaining abstinence and drinking reduction was investigated. Their application to other aspects usually associated with alternative therapies in this topic area (such as craving and withdrawal symptoms) was beyond the scope of this guideline and hence was not investigated. Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3.

Table 81. Clinical review protocol for the review of Meditation.

Electronic databases	COCHRANE, AMED, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs (≥ 10 participants per arm); Systematic Reviews
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Meditation
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

Notes.

6.19.3 Studies considered for review

The review team conducted a systematic search of RCTs and systematic reviews that assessed the beneficial or detrimental effects of meditation in the treatment of alcohol dependence or harmful alcohol use. Following the literature search, there was an insufficient number of studies remaining to perform an unbiased and comprehensive meta-analysis of meditation for the treatment of AUDs. Therefore, the GDG consensus was that a narrative summary of these studies would be conducted and observational studies would be included in the review. See Table 53 for a summary of the study characteristics.

Two trials (Bowen *et al*., 2006[32]; Zgierska *et al*., 2008) relating to clinical evidence providing data on n=320 participants were identified by the search. Both studies were published in peer-reviewed journals between 2006 and 2008. To our knowledge, no other studies which evaluated meditation for an AUD population with alcohol-focused outcomes have been published. See Table 53 for study characteristics.

[32] A secondary analyses of this ample was conducted by Bowen *et al.* (2007).

Table 82. Summary of study characteristics for Mindfulness Meditation

Study (Country)	Treatment Conditions & Number of Participants	Baseline Severity & Diagnosis	Setting, Treatment Characteristics & Assessment Points
BOWEN2006 (USA)	1.Mindfullness Meditation (n=63) 2.Treatment As Usual (n=242)	*No indication of level of dependence *Baseline drinks per week Meditation group = 64.83 (SD=73.01); TAU = 43.98 (SD=55.61)	**Setting:** Prison **Treatment Characteristics: Meditation:** 10-day course, **TAU:** chemical dependency treatment, psychoeducational intervention **Assessment Point:** at 3 months after release from prison
ZGIERSKA2008 (USA)	1.Mindfulness Meditation (n=19). Participants continued usual outpatient treatment	*DSM-IV alcohol-dependent graduates from an intensive outpatient treatment program	**Setting:** Alcohol Treatment Centre **Treatment Characteristics:** 8-week course, 2-hour weekly sessions; Course involved both meditation training and relapse prevention using cognitive behavioural techniques. **Assessment Points:** 4, 8, 12, 16 week post-baseline

6.19.4 Evidence Summary

Bowen *et al.* (2006) investigated the effectiveness of mindfulness meditation on substance use outcomes in an incarcerated population. The study compared mindfulness meditation with treatment-as usual (chemical dependency program and psychoeducational intervention). The authors reported that mindfulness meditation was significantly more effective than treatment as usual in the amount of alcohol consumed at 3 month follow-up ($p<0.005$). However, adherence to the therapy was not assessed and therefore the authors were unclear as to whether participants correctly followed the principles of mindfulness meditation. Furthermore, the level of alcohol dependence in this sample was unclear.

In a feasibility pilot prospective case series study, Zgierska *et al.* (2008) evaluated the efficacy of mindfulness meditation in increasing abstinence and reducing the quantity of alcohol consumed. Alcohol dependent participants whom had recently completed an intensive outpatient treatment program were recruited. The study found that participants reported significantly fewer heavy drinking days at 4, 8 and 12 week follow-up (all $p<0.005$) but not 16 week follow-up. Furthermore, participants were drinking significant less when assessed at 4 and 8 week follow-up ($p<0.005$) but no significant difference was observed at 12 and 16 week follow-up. No significant difference over time was observed in increasing percent days abstinent. It must be noted however, that meditation in this study was not used as an active intervention but an after treatment intervention. Furthermore, the sample size was small and the study had no control group.

These studies reported a significant effect of mindfulness meditation on alcohol consumption Overall, there is limited and poor quality evidence which does not support the use of mindfulness-based meditation for treating alcohol dependence and harmful alcohol use.

6.20 Clinical evidence summary

A range of psychological interventions to prevent relapse or promote abstinence in harmful and dependent alcohol misuse were reviewed. These included: cognitive behaviour therapies, social behavioural and network therapies, behavioural therapies (including cue response), twelve-step facilitation and motivational techniques. For all the above interventions the evidence was judged to be of a high or moderate quality on the GRADE profiles. Evidence for efficacy showed an advantage for behavioural couples therapy both over treatment as usual, active controls and other active interventions. In the cases of the other psychological interventions there was evidence that CBT, social behaviour and networks therapy and behavioural therapies were better than treatment as usual. In the case of twelve-step facilitation and motivational techniques, although there was evidence to equivalents to other interventions, there was no evidence to show that these interventions were, for harmful and dependent drinkers, more effective than the other interventions, and importantly there was a lack of evidence for their effectiveness compared to treatment as usual.

In addition, the GDG felt that both motivational techniques and twelve-step facilitation were best seen as components of any effective psychosocial intervention delivered in alcohol services with the assessment and enhancing of motivation

forming a key element of the assessment process. It should also be noted that facilitation of uptake of community support (for example, Alcoholics Anonymous) is also seen as a key element of case coordination and case management (see Chapter 5). It should also be noted that the individual psychological interventions form a required component part of any pharmacological intervention and in developing these recommendations this was also borne in mind.

6.21 Health economic evidence

6.21.1 Review overview

The literature search identified four studies that assessed the cost-effectiveness of psychological interventions for the treatment of alcohol dependence or harmful alcohol use (Alwyn *et al.,* 2004; Mortimer & Segal 2005; Slattery *et al.,* 2003; UKATT study, 2005). Full references, characteristics and results of all studies included in the economic review are presented in the form of evidence tables in the appendices.

The study by Alwyn and colleagues (2004) considered the cost-effectiveness of adding a psychological intervention (PI) to a conventional home detoxification programme for the treatment of problem drinkers. The home detoxification programme comprised five home visits of 30 minutes duration delivered by community psychiatric nurses (CPNs). The study population consisted of 91 heavy drinkers in the UK who fulfilled inclusion criteria for home detoxification. A number of outcome measures were assessed in the study including: number of drinks per drinking day; total number of days abstinent; total number of alcohol units consumed; abstinence or moderate drinking and severity of dependence. The number-needed-to-treat (NNT) to produce one extra non-drinker was also calculated. An NHS perspective was used for the economic analysis. Resource use data included inpatient days, outpatient care (including CPN visits) and medications. As clinical outcomes were left disaggregated and no summary outcome measure was used in the economic analysis, a cost-consequences analysis was used.

The authors made no formal attempt to compare the total costs of PI in addition to home detoxification versus home detoxification alone. Instead the authors calculated total costs per patient of inpatient treatment (£2,186 to £3,901), outpatient treatment (£581 to £768) and home detoxification plus PI (£231). Therefore, the extra cost of a PI programme was substantially lower than the cost of inpatient treatment and outpatient visits. In terms of clinical outcomes, significantly better results were observed in patients treated with home detoxification plus PI. The authors concluded that, due to the low NNT to obtain an extra non-drinker, it is likely that the implementation of a PI would lead to cost savings to the NHS. Although the results of this study are highly relevant to the UK context, there are a number of methodological limitations. Firstly, no attempt was made to combine costs and effectiveness with an array of effectiveness measures used in the study. The measures of effectiveness used are of limited usefulness to policy-makers when assessing the comparative cost-effectiveness of health care interventions. The clinical effectiveness study compared PI in addition to home detoxification versus home detoxification alone. However, in the cost-analysis, home detoxification was compared with other detoxification programmes, such as inpatient and outpatient programmes. Therefore, the study did not directly assess the cost-effectiveness of adding PI to home detoxification.

The study by Mortimer and Segal (2005) conducted separate, mutually exclusive model-based economic analyses of interventions for problem drinking and alcohol dependence. A lifetime horizon was used for all of the analyses considered. The first analysis compared three brief motivational interventions with different levels of intensity (simple = 5min, brief = 20min or extended = 4 sessions x 120-150min) versus no active treatment in a population of heavy drinkers within the Australian health care setting. The outcome measure used in the analysis were QALYs calculated from disability weights derived from a single published source (Stouthard *et al*. 1997). Clinical effectiveness data was taken from published studies evaluating interventions targeting heavy drinkers at lower severity levels. This data was used to estimate how patients would progress between specific drinking states (problem, moderate or dependent) within the model. The authors did not specify the resource use and cost components included in the model within the article although a health service perspective was adopted for the analysis. The results of the analysis suggested that brief motivational interventions were cost-effective compared to no active treatment. The incremental cost-effectiveness ratios (ICERs) ranged from under $AUD 82 per QALY for the simple intervention to under $AUD 282 per QALY for the extended intervention.

The second analysis compared psychotherapies for mild to moderate alcohol dependence. The comparators were moderation-oriented cue exposure (MOCE) versus behavioural self-control training (BSCT) and motivational enhancement therapy (MET) or non-directive reflective listening (NDRL) versus no further counselling after initial assessment (NFC), again within the Australian health care setting. Again, the outcome measure used in the analysis were QALYs calculated from disability weights derived from a single published source (Stouthard *et al*. 1997). Clinical effectiveness data was taken from published studies evaluating interventions for mild to severely dependent drinkers. This data was used to estimate how patients would progress between specific drinking states (problem, moderate or dependent) within the model. No resource use and cost components were specified within the article. The results of the analysis suggested that MOCE was cost-effective in comparison to BSCT, resulting in an ICER of $AUD 2145 per QALY. NDRL was dominated by NFC, resulting in higher costs but lower QALYs. However, the results of the analysis suggested that MET was cost-effective compared to NFC, resulting in an ICER $AUD 3366 per QALY.

There are several limitations with the results of the study by Mortimer & Segal (2005) that reduce their applicability to any UK-based recommendations. In the second analysis of interventions for mild to moderate alcohol dependence, a common baseline comparator was not used in the analyses of MOCE, MET and NDRL, limiting their comparability in terms of cost-effectiveness. Ideally, indirect comparisons of the three interventions would have provided additional information about their relative effectiveness. Little explanation was given in the article as to how the clinical effectiveness data, which was taken from various sources, was used to inform the health states used in the economic models. The article did not specify the resource use and costs that were included in the analyses although a health perspective was used. The analyses all used QALYs as the primary outcome measure, which allows for comparison across interventions, although again there

was insufficient description of the utility weights that were applied to the health states within the model.

The study by Slattery and colleagues (2003) developed an economic model to assess the cost-effectiveness of four psychological interventions in comparison to standard care within the Scottish health service: Coping/Social Skills Training; Behavioural Self-Control Training (BSCT); Motivational Enhancement Therapy (MET) and Marital/Family Therapy. The population examined were 45-year old men and women with a diagnosis of alcohol dependence. The outcome measures used in the economic model were the number of patients who have abstained and number of patient deaths averted. The clinical effectiveness data was based on a methodologically diverse selection of trials which were not described within the study. Most studies included a treatment arm in which the intervention was thought likely to have little or no effect and this was used as the comparator arm when available. Resource use involved in the delivery of psychosocial therapies was estimated from expert clinical opinion and included the number and duration of sessions; staff and educational materials. Unit costs were taken from Scottish health service estimates. Other health care costs included in the model were those associated with alcohol-related disease endpoints such as stroke, cancer, cirrhosis and alcohol-related psychoses. Costs were applied according to inpatient length of stay taken from Scottish medical records.

For each intervention, the costs of psychosocial treatment and any disease endpoints for a hypothetical cohort of 1000 patients were compared with standard care over a 20 year time horizon, to determine any net health care cost savings. All four therapies demonstrated net savings ranging from £274,008 (Coping/Social Skills Training) to £80,452 (BSCT) in comparison to standard care. All four interventions resulted in lower costs per additional abstinent patient and lower costs per death averted in comparison to standard care. Whilst the results of the study, based on a hypothetical cohort of patients within the Scottish health service, may be applicable to a UK setting, there are several problematic methodological issues with the study. Firstly, the sources of the effectiveness data used in the model were not explicitly described by the authors who suggested that the data was taken from a methodologically diverse selection of trials, thus suggesting a high level of heterogeneity. Secondly, no attempt was made to translate intermediate clinical endpoints such as abstinence rates into Quality-Adjusted Life Years (QALYs), which are useful to decision makers when assessing the comparative cost-effectiveness of health care interventions.

The UKATT study (2005) evaluated the cost-effectiveness of motivational enhancement therapy (MET) versus social behaviour and network therapy amongst a population comprised of people who would normally seek treatment for alcohol problems at UK treatment sites. The outcome measure used in the economic analysis were QALYs which were estimated by using the EQ-5D questionnaire completed by patients at baseline, 3 and 12 months. The primary measures of clinical effectiveness were changes in alcohol consumption, alcohol dependence and alcohol-related problems over the 12-month period. A societal perspective was taken for the analysis. Resource use data that was collected during the study included training and supervision and materials related to treatment, hospitalisation, outpatient visits, GP and CPN visits, rehabilitation and consultation in alcohol agencies, social service

contacts and court attendances. Unit cost estimates were derived from a variety of UK published sources.

At 12 months, the total mean costs were higher in the MET group, resulting in a mean difference of £206 per patient (95% CI -£454 to £818) versus social behaviour and network therapy. After adjusting for baseline differences, the MET group achieved slightly higher QALYs than social behaviour and network therapy, resulting in a mean difference of 0.0113 QALYs (95% CI: -0.0532 to 0.0235). Combining costs and QALYs, the MET group had an incremental cost-effectiveness ratio of £18,230 in comparison with social behaviour and network therapy. Cost-effectiveness acceptability curves showed that, at a cost-effectiveness threshold of £30,000 per QALY, MET had a 57.6% probability of being more cost-effective than social behaviour and network therapy. The results of the study are applicable to a UK setting and the outcome measure used enables comparison across health care interventions. However, as the authors note, the analysis had a short time horizon and the longer term effects of a reduction in drinking were not taken into consideration.

6.21.2 Health economic summary

The systematic search of the health economics literature did not identify evidence on the cost effectiveness of all of the psychological interventions considered in this guideline. Three of the studies identified were UK-based (Alwyn *et al.* 2004; Slattery *et al.* 2003; UKATT study, 2005) and one was Australian (Mortimer & Segal, 2005). The study by Alwyn and colleagues (2004) suggested that adding psychological intervention to a home detoxification programme may offer NHS cost savings in problem drinkers. The study by Slattery and colleagues (2003) showed that four psychological interventions, including coping/social Skills training; behavioural self-control training (BSCT); motivational enhancement therapy (MET) and marital/family therapy offered significant health care cost savings compared to standard care for alcohol-dependent patients. The UKATT study (2005) suggested that motivational enhancement therapy was cost-effective in patients with alcohol problems, at current UK thresholds, in comparison to social behaviour and network therapy (but note it was identified as a clinically effective intervention in this guideline). Mortimer and Segal (2005) concluded that brief motivational interventions were cost-effective compared to no active treatment among problem drinkers whilst moderation-oriented cue exposure (MOCE) and MET were cost-effective treatments for alcohol dependency, although no common comparators were used in either analysis.

Providing an adequate summary of the health economics evidence presented here is difficult, due to the differences across the studies in terms of the interventions and comparators considered, study populations, costs and outcomes considered and other methodological differences. Overall, the health economics review does not provide evidence of superior cost effectiveness for any particular psychological therapy.

6.21.3 Economic considerations

Of all the psychological interventions included in the systematic effectiveness review and then found suitable for recommendation in the NHS, only a few of these have supporting economic evidence.

A potential solution to this problem would be to undertake economic modelling to determine the most cost effective psychological intervention. However, certain aspects of the effectiveness evidence made it difficult to do so i.e. there was a lack of common comparators and interventions were usually compared to other active interventions, a 'no treatment/usual care/placebo' arm was rarely identified.

Furthermore, the meta-analyses showed that there were small if any differences in effect between active treatments, and only a few of these showed much evidence a consistent positive effect e.g. behavioural couples therapy, particularly against other therapies. .

Therefore the following costing exercise was undertaken for the possible recommended psychological interventions.

Behavioural Couples Therapy

The clinical effective studies in the guideline systematic literature review described this intervention being delivered in a variety of ways. The GDG were of the opinion that the number of sessions and duration of these sessions as described by Lam and colleagues (2009) i.e. 12 weekly session of 60 minutes duration under the supervision of a competent practitioner, were considered to be reflective of what should be delivered in the UK NHS.

It is very likely that these sessions would be conducted by a clinical psychologist. The unit cost of a clinical psychologist is £75 per hour of patient contact in 2008/09 prices (Curtis, 2009). This cost includes salary, salary on-costs, overheads and capital overheads plus any qualification costs.

Based on these estimates the average cost of a behavioural couples therapy intervention would be £900 per couple.

Cognitive Behavioural Therapy (CBT)

No evidence on the cost effectiveness of cognitive behavioural therapy in this population was identified by the systematic search of the health economics literature.

The clinical evidence in the guideline systematic literature review described CBT interventions being delivered in a variety of sessions and durations either individually or in structured groups under the supervision of a competent practitioner. The clinical evidence was taken in consideration and the GDG agreed that a CBT programme would typically involve weekly sessions of 1 hour duration over a 12 week period.

These sessions would be conducted by a clinical psychologist. The unit cost of a clinical psychologist is £75 per hour of patient contact in 2008/09 prices (Curtis, 2009). This cost includes salary, salary oncosts, overheads and capital overheads plus any qualification costs.

Based on these estimates the average cost of an individual based CBT intervention would be £900 per patient.

The GDG were of the opinion that group interventions although likely to be more cost effective per patient, they were unlikely to be delivered successfully in an outpatient setting because of the expected high attrition/low retention rates. They were also of the opinion that group interventions would potentially be more suitable to inpatient/residential settings as the likelihood of patients attending all treatment sessions would be higher. It was unclear from the literature what the optimal number of patients per group would be. Obviously, if the number and duration of sessions as well as the number of staff delivering the service remained the same, the total costs per person would be expected to decrease significantly.

Social Network & Environment Based Therapies

The UKATT Research team described social behaviour and network therapy to comprise of up to eight 50-minute sessions (UKATTstudy, 2005). This particular intervention can be delivered by a range of mental health professionals. The GDG highlighted that it is likely that the sessions would be supervised by a nurse (or a NHS professional who is trained to deliver this intervention). It was assumed that such workers would be on Agenda for Change (AfC) salary scale 6 which would likely to be comparable to the salary scales of a community nurse. The unit cost of an AfC Band 6 community nurse is £70 per hour of patient contact in 2008/09 prices (Curtis, 2009). This cost includes salary, salary oncosts, overheads and capital overheads plus any qualification costs. Based on these estimates the average cost of such a therapy would be £467 per patient.

Behavioural Therapies

The clinical evidence in the guideline systematic literature review described a variety of interventions that were considered to be behavioural therapies. They were delivered in a variety of sessions and durations either individually or in structured groups under the supervision of a competent practitioner. The clinical evidence was taken in consideration and the GDG agreed that behavioural therapies would typically involve weekly sessions of 1 hour duration over a 12 week period.

Behavioural therapies can also be delivered by a range of mental health professionals. The GDG highlighted the following professionals: a clinical psychologist or a nurse or a NHS professional who is trained to deliver this intervention. It was assumed that such workers would be on Agenda for Change (AfC) salary scale 6 which would likely to be comparable to the salary scales of a community nurse. The unit cost of an AfC Band 6 community nurse is £70 per hour of patient contact and the unit cost of a clinical psychologist is £75 per hour of patient contact in 2007/08 prices (Curtis, 2008). These costs include salary, salary oncosts, overheads and capital overheads plus any qualification costs. Based on these estimates the average cost of a behavioural intervention would be £900 per patient if delivered by a clinical psychologist and £840 per patient if delivered by a mental health professional described above.

A summary of the estimated resource use and costs involved in delivering these psychological interventions is presented in Table 54.

Table 83. Summary of resource use and costs associated with psychological interventions

Behavioural Couples Therapy	***£ 900 per couple***
12 weekly sessions 60 minutes long	this estimate based on LAM, 2009 (study included in clinical evidence review)

Clinical Psychologist	£75 per hour of client contact (Curtis, 2009)	
Cognitive Behavioural Therapy	***£ 900 per patient***	
12 weekly sessions 60 minutes long	GDG expert opinion and clinical evidence	
Delivered by clinical psychologist	£75 per hour of client contact (Curtis, 2009)	
Social Network & Environment Based Therapies		
8 sessions 50 minutes long	UKATT study, (2005)	
nurse(community)	AfC Band 6 £70/hr spent with patient (£1.17/min)	***£467 per patient***
Behavioural Therapies		
12 weekly sessions 60 minutes long	GDG expert opinion and clinical evidence	
Clinical Psychologist	£75 per hour of client contact (Curtis, 2009)	***£ 900 per patient***
nurse(community)	AfC Band 6 £68/hr spent with patient £1.13/min	***£816 per patient***

6.21.4 From evidence to recommendations

As we can see from the above evidence summary, the strongest evidence for effectiveness in harmful and dependent drinking was for behavioural couples therapy. It is therefore recommended that behavioural couples therapy be considered as an effective intervention for individuals with harmful and mildly dependent alcohol misuse that had a partner, who was willing to engage in treatment. Behavioural couples therapy should be offered for mild dependent and harmful drinkers as a standalone intervention. Consideration should also be given to giving behavioural couples therapy in combination with a pharmacological intervention for those individuals who meet the above criteria and have moderate or severe alcohol dependence (see Chapter 6).

The evidence for individual psychological interventions for harmful and mildly dependent drinkers was limited but stronger for CBT, social network and behaviour therapy and behaviour therapy than other therapies reviewed and are therefore recommended. The GDG considered the costings of the various psychological interventions (indications from this costings was that social network behaviour therapy was less costly than either CBT or behaviour therapy) but considered that, given the uncertainty about the relative cost-effectiveness of the interventions and the need to have available a range of interventions to meet the complexity of presenting problems that all three interventions should be recommended as standalone interventions. One of the three interventions should also used in combination with the drug treatments reviewed in Chapter 6.

As can be seen from the clinical summary the GDG considered that TSF and motivational-based interventions should be provided as the evidence, particularly against treatment as usual or similar controls was not strong enough to support their use as a standalone intervention for harmful and mildly dependent drinkers who seek treatment.

6.21.5 Recommendations

6.21.5.1 For all people who misuse alcohol, carry out a motivational intervention as part of the initial assessment. The intervention should contain the key elements of motivational interviewing including:

- helping people to recognise problems or potential problems
- helping to resolve ambivalence and encourage positive change and belief in the ability to change
- adopting a persuasive and supportive, rather than an argumentative and confrontational, position.

6.21.5.2 For all people who misuse alcohol, offer interventions to promote abstinence or moderate drinking as appropriate (see 5.22.1.8) and prevent relapse, in community-based settings.

6.21.5.3 Consider offering interventions to promote abstinence and prevent relapse as part of an intensive structured community-based intervention for people with moderate and severe alcohol dependence who have:

- very limited social support
- complex physical or psychiatric comorbidities
- not responded to initial community-based interventions. **[KPI]**

6.21.5.4 All interventions for people who misuse alcohol should be delivered by competent staff. Psychological interventions should be based on a relevant evidence-based treatment manual, which should guide the structure and the duration of the intervention. Staff should consider using competence frameworks developed from the relevant treatment manuals and for all interventions should:

- receive regular supervision from individuals competent in both the intervention and supervision
- routinely use outcome measurements to make sure that the person who misuses alcohol is involved in reviewing the efficacy of treatment
- engage in monitoring and evaluation of treatment adherence and practice competence, for example, by using video and audio tapes and external audit and scrutiny if appropriate. **[KPI]**

6.21.5.5 All interventions for people who misuse alcohol should be the subject of routine outcome monitoring. This should be used to inform decisions about

continuation of both psychological and pharmacological treatments. If there are signs of deterioration or no indications of improvement, consider stopping the current treatment and review the care plan.

6.21.5.6 For all people who misuse alcohol who are receiving an intervention:

- give information on the value and availability of community support networks and self-help groups (for example, Alcoholics Anonymous)
- help them to participate in these services, for example by arranging support to attend meetings.

Interventions for harmful drinking and mild alcohol dependence

6.21.5.7 For harmful drinkers and people with mild alcohol dependence, offer a psychological intervention (such as cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol-related cognitions, behaviour, problems and social networks. **[KPI]**

6.21.5.8 For harmful drinkers or people with mild alcohol dependence, offer behavioural couples therapy to service users who have a regular partner and whose partner is willing to participate in treatment.

6.21.5.9 For harmful drinkers or people who are mildly dependent on alcohol and who have not responded to psychological interventions alone, or who have specifically requested a pharmacological intervention, consider offering acamprosate[33] or oral naltrexone[34] in combination with an individual psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) or behavioural couples therapy (see chapter 7 for pharmacological interventions and chapter 6 for psychological interventions).

Delivering psychological interventions

6.21.5.10 Cognitive behavioural therapies focused on alcohol-related problems should typically consist of one 60-minute session per week for 12 weeks.

6.21.5.11 Behavioural therapies focused on alcohol-related problems should typically consist of one 60-minute session per week for 12 weeks.

6.21.5.12 Social network and environment-based therapies focused on alcohol-related problems should typically consist of eight 50-minute sessions over 12 weeks.

[33] Note that the evidence for acamprosate in the treatment of harmful drinkers and people who are mildly alcohol dependent is less robust than that for naltrexone.

[34] At the time of publication (June 2010), naltrexone did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented.

6.21.5.13 Behavioural couples therapy should be focused on alcohol-related problems and their impact on relationships. It should aim for abstinence, or a level of drinking predetermined and agreed by the therapist and the service user to be reasonable and safe. It should typically consist of one 60-minute session per week for 12 weeks.

6.21.6 Research recommendation

6.21.6.1 Is contingency management compared with standard care effective in reducing alcohol consumption in people who misuse alcohol?

This question should be answered using a randomised controlled design that reports short-and medium-term outcomes (including cost-effectiveness outcomes) of at least 18 months' duration. Particular attention should be paid to the reproducibility of the treatment model and training and supervision of those providing the intervention to ensure that the results are robust and generalisable. The outcomes chosen should reflect both observer and service user-rated assessments of improvement and the acceptability of the intervention. The study needs to be large enough to determine the presence or absence of clinically important effects, and mediators and moderators of response should be investigated.

Why this is important?

Psychological interventions are an important therapeutic option for people with alcohol related problems. However, even with the most effective current treatment (e.g. cognitive behavioural therapies and social network and environment-based therapies), the effects are modest at best and the treatments are not effective for everyone. Contingency management has a considerable and compelling evidence base in the treatment of substance misuse (e.g. opioid misuse) but there is only a limited, if promising, evidence base for contingency management in the treatment of alcohol- related problems. The results of this research will have important implications for the provision of psychological treatment for alcohol misuse in the NHS.

6.22 Acupuncture

Introduction

Acupuncture is a form of Chinese medicine which has been practiced for over 3000 years (Jordan, 2006). It involves inserting fine needles at selected points on the skin to balance the body's energy (chi), with the aim of treating and preventing disease. Acupuncture was introduced specifically for use in the treatment of substance-related disorders approximately 30 years ago (Kao, 1974; Leung, 1977; Sacks, 1975; Wen *et al*., 1973). However, research has predominantly been for drug addictions for example, opiate dependence (Jordan, 2006), cocaine dependence (Gates *et al*., 2006; Mills *et al*., 2005) as well as nicotine dependence (White *et al*. 2006). Research for the

use of acupuncture in alcohol use disorders is rather more limited and to date there are only two systematic reviews of acupuncture for alcohol dependence (Cho & Whang, 2009; Kunz *et al*., 2004). Addiction-specific auricular acupuncture involves inserting five small needles on each ear at points regarded to be specific to chemical dependence (shenmen, 'sympathetic', 'kidney', 'liver' and 'lung') (Smith and Khan, 1988; Wen, 1979).

6.22.1 Clinical review protocol

In the current review, the role of acupuncture in maintaining abstinence and drinking reduction was investigated. Its application to other aspects usually associated with alternative therapies in this topic area (such as craving and withdrawal symptoms) was beyond the scope of this guideline and hence was not investigated. Information about the databases searched and the inclusion/ exclusion criteria used for this Section of the guideline can be found in Chapter 3. The GDG were of the opinion that a search for RCT studies alone may result in an insufficient number of studies to perform a review, therefore a consensus-based decision was made to also search for systematic reviews.

Table 84 Clinical review protocol for the review of Acupuncture

Electronic databases	COCHRANE, AMED, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Systematic Reviews from 1993 to March 2010. All other searches from database inception to March 2010
Study design	RCTs (≥ 10 participants per arm); Systematic Reviews
Patient population	Adults (>18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking >30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant Women
Interventions	Acupuncture (all types)
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

6.22.2 Studies considered for review

The review team conducted a systematic search of RCTs and published systematic reviews that assessed the beneficial or detrimental effects of acupuncture in the treatment of alcohol dependence or harmful alcohol use. Following the literature search, 11 primary studies were identified. Of these studies, 4 investigated the effects of acupuncture on withdrawal symptoms, and 2 assessed its use for the management of cravings. These studies were excluded as the outcomes are outside the scope of this guideline. Therefore, five studies (4 RCTs, 1 observational study) were identified for inclusion in a review. However, the review team could not perform an unbiased and comprehensive meta-analysis as there were inconsistent outcomes measures across studies. Therefore, the GDG consensus was that a narrative summary of these studies would be conducted. The studies included for review were Bullock *et al*.,

(1987) (addiction-specific vs. non-specific acupuncture); Bullock *et al*., (1989) (addiction-specific vs. non-specific acupuncture); Worner (1992) (addiction specific acupuncture vs. sham transdermal stimulations vs. standard care control); Rampes (1997) (addiction-specific vs. non-specific acupuncture vs. no treatment control); and Bullock (2002) (addiction specific acupuncture vs. symptom-based acupuncture vs. non-specific acupuncture vs. standard care control). These studies were conducted between 1987 and 2002 and provided data on n=752 participants. See Table 56 for characteristics of these studies. All included studies were RCTS bar Bullock *et al.,* (1989).

Table 85. Summary of study characteristics for Acupuncture

Study (Country)	Treatment Conditions & Number of Participants	Baseline Severity & Diagnosis	Setting, Treatment Characteristics & Assessment Points
Bullock 1987 (USA)	1. Addiction Specific Acupuncture (n=27)	* 98.1% of sample indicated alcohol as single substance of abuse	**Setting:** Alcohol Treatment Centre
	2. Non-addiction specific Acupuncture (control) (n=27)	* Mean years of alcohol abuse: Treatment group = 21.6; Control group = 18.5	**Treatment Characteristics:** 45 day standard acupuncture treatment
	*Auricular and hand acupuncture	* 68.5% of sample drink daily; 27.7% binge drink	**Assessment Points:** No follow up, assessing during different phases of treatment
Bullock 1989 (USA)	1. Addiction Specific Acupuncture (n=40)	*Alcohol dependent participants	**Setting:** Alcohol Treatment Centre
	2. Non-addiction specific Acupuncture (control) (n=40)	* Mean years of alcohol abuse: Treatment group = 23.2; Control = 20.8	**Treatment Characteristics:** Patients received treatment after 3-5 day withdrawal management
	*Auricular and hand acupuncture	* 71% of the sample drink daily; 21% binge drink	**Assessment Points:** 1, 3 & 6 month follow up
Worner 1992 (USA)	1. Addiction Specific Acupuncture (n=19)	*Alcohol dependent participants	**Setting:** Alcohol Treatment Centre
	2. Needleless Transdermal Stimulation (control) (n=21)	* Daily intake approx 253.6 g/day	**Treatment Characteristics:** 3 month treatment; all participants received standard care (individual and group counselling, AA, task-oriented group activities)
	3. Standard Care Control (n=16)		**Assessment Points:** 3 month follow up
	*Acupuncture at various body parts		
Rampes1997 (UK)	1. Addiction Specific Electro Auricular Acupuncture (n=23)	* DSM-III-R alcohol dependent or abuse	**Setting:** Alcohol Treatment Centre
	2. Non-addiction specific Electro Auricular Acupuncture (control) (n=20)	* SADQ score approx 32 across groups	**Treatment Characteristics:** 30 mins per week for 6 weeks;
	3. No Treatment Control (n=16)		Assessment Points: 2 & 6 month follow up
	*Auricular Acupuncture		
Bullock 2002 (USA)	1. Addiction Specific Auricular Acupuncture (n=132)	*Alcohol dependent participants in a residential treatment facility	Setting: Alcohol Treatment Centre
	2. Symptom-based Auricular Acupuncture (n=104)		Treatment Characteristics: 3 cycles of 6 treatments for 3 weeks
	3. Non-addiction specific Acupuncture (control) (n=133)		Assessment Points: 3, 6, & 12 month follow-up
	4. Standard Care Only – Minnesota Model (control) (n=134)		
	*Auricular Acupuncture		

6.22.3 Evidence summary

Bullock *et al.,* (1987) investigated acupuncture at addiction specific points versus non-specific points for reducing craving and maintaining abstinence. The authors report that the treatment group had significantly fewer drinking episodes than the control group ($p=0.007$) after the second (28 days) and third (45 days) phase of treatment but not after the first phase (5 days).

Bullock *et al.*, (1989) also investigated acupuncture at addiction specific points versus non-specific points for craving reduction, maintaining abstinence and drinking reduction in chronic alcohol abusers. The study found that there was no significant difference between the treatment group and control group at 1 month follow-up in the number of drinking episodes (consumption of more than 3 drinks in one period). However at both three and six month follow up, the treatment group reported significantly less drinking episodes than the control group ($p<0.001$). Furthermore, the treatment group was significantly more effective than control at maintain abstinence and controlled drinking goals when assessed at one month ($p<0.01$) three and six month follow-up (both $p<0.05$). This study was not randomized however; hence the results must be viewed with caution.

Worner (1992) evaluated at addiction specific points versus needleless transdermal stimulation as well as a standard care group who receive no acupuncture. This study found no significant difference between groups in the number of participants who relapsed or needed further withdrawal management at three month follow-up.

Rampes (1997) assessed addiction specific electro-acupuncture versus non-specific electro-acupuncture and no treatment (control). The main outcome of interest was craving reduction which is outside the scope of this guideline. However, the authors also reported no significant difference between groups in amount of alcohol consumed at 2 and 6 month follow-up.

Bullock (2002) investigated specific and non-specific acupuncture as well as symptom-based acupuncture and standard care (based on the Minnesota Model). The authors found no significant difference in alcohol consumption at 3, 6 and 12 month follow-up. Overall, the evidence suggests that acupuncture is not effective in drinking reduction and maintaining abstinence.

The results of these studies are conflicting and show both a benefit of addiction-specific acupuncture as well as no difference between addiction-specific acupuncture and other control conditions. Additionally, the treatments across studies are not comparable as the studies used different body parts for acupuncture treatment, different types of control group, different length of treatment and follow-up and varied significantly in sample size. Although the quality of these trials are acceptable in the most part, the number of studies are limited and there is not enough evidence to confirm the benefit of acupuncture in maintaining abstinence or reducing the amount of alcohol consumed. Therefore no recommendations are made.

6.22.4 Research recommendation

6.22.4.1 Is acupuncture compared with usual care effective in reducing alcohol consumption?

This question should be answered using a randomised controlled design that reports short-and medium-term outcomes (including cost-effectiveness outcomes) of at least 12 months' duration. Particular attention should be paid to the reproducibility of the treatment model and training and supervision of those providing the intervention to ensure that the results are robust and generalisable. The outcomes chosen should reflect both observer and service user-rated assessments of improvement and the acceptability of the treatment. The study needs to be large enough to determine the presence or absence of clinically important effects, and mediators and moderators of response should be investigated.

Why this is important?

Non-pharmacological treatments are an important therapeutic option for people with alcohol-related problems. There is an evidence base for acupuncture in reducing craving but not alcohol consumption in a number of small trials. The evidence for pharmacological treatments (e.g. acamprosate or naltrexone) and psychological treatments (e.g. cognitive behavioural therapies and social network and environment-based therapies) is modest at best and the treatments are not effective for everyone. Anecdotal evidence suggests that acupuncture, like psychological treatment, is valued by service users both in alcohol misuse and substance misuse services (although the evidence base for effectiveness is weak). The results of this study will have important implications for increased treatment choice for people who misuse alcohol in the NHS.

6.23 Psychological interventions for carers

6.23.1 Introduction

There is an increasing recognition that alcohol misuse affects the entire family and the communities in which these families live but what constitutes best practice in the area is not well understood (Copello *et al*, 2006). What is not in doubt is the considerable suffering and hardship experienced by many families where a family member has a significant alcohol problem (ref).

In developing this guideline the GDG drew on a previous review of psychological interventions for carers which had been undertaken for the NICE guideline on Psychosocial Interventions for Drug Misuse (NCCMH, 2008). This was a pragmatic decision as the previous review had drawn on literature covering both drug misuse and alcohol misuse and searches conducted for this guideline had failed to find any substantial new evidence from interventions to support family members and carers. The outcome of the NCCMH (2008) review is summarised below in narrative form.

The NCCMH (2008) guideline identified a number of interventions in the drug and alcohol field that had been developed and tested in formal trials. They are listed below

5-Step intervention

The 5-Step intervention seeks to help families and carers in their own right, independent of relatives who misuse drugs or alcohol. It focuses on three key areas: stress experienced by relatives, their coping responses and the social support available to them. Step 1 consists of listening and reassuring the carer, Step 2 involves providing relevant information, Step 3 counselling about coping, Step 4 counselling about social support and Step 5 discussion of the need for other sources of specialist help. This intervention consists of up to five sessions.

Community reinforcement and family training

Community reinforcement and family training is a manualised treatment programme that includes training in domestic violence precautions, motivational strategies, positive reinforcement training for carers and their significant other, and communication training. However, the primary aim of the treatment appears to be encouraging the person who misuses drugs or alcohol to enter treatment. This intervention again consists of up to five sessions.

Self-help support groups

A group of families and carers of people who misuse drugs meets regularly to provide help and support for one another.

Guided self-help

A professional offers a self-help manual (for example, based on the 5-Step intervention), provides a brief introduction to the main sections of the manual and encourages the families and/or carers of people who misuse drugs to work through it in their own time at home.

6.23.2 Summary of the 2008 review

The review identified a total of three RCTs including two trials (Kirby *et al.*, 1999; Meyers *et al.*, 2002) for community reinforcement and family training CRFT) where was compared to 12 Step self-help groups and one trial one trial (Copello *et al.*, 2009[35]) of the 5-Step intervention in which 5-Step interventions of various intensities were compared.

In CRFT neither study reported any benefit on the indentified family meters drug or alcohol problems. However, Kirby and colleagues (1999) found statistically significant changes from baseline for both groups in relation to carer problems and psychological functioning. In contrast, Meyers and colleagues (2002) found no statistically significant differences (after Bonferroni corrections for multiple testing) in changes from baseline at 12-month follow-up. In the case of the 5-step intervention Copello and colleagues (2007) on two primary outcomes related to physical and psychological health and coping. No statistically significant differences were found between the full intervention and the guided self-help conditions for both physical and psychological health (WMD - 0.23; 95% CI, -4.11 to 3.65) and coping (WMD -0.12; 95% CI, -5.42 to 5.19).

[35] Note this trial was identified prior to publication in 2008 but the reference to the published trial is used here.

6.23.3 Clinical summary

For both community reinforcement and family training and 5-step intervention, there were no statistically significant differences found between these more intensive interventions and self-help (that is, 12-step self-help groups and guided self-help). It appears that self-help interventions are as effective as more intensive psychological interventions in reducing stress and improving psychological functioning for carers and families of people who misuse drugs and alcohol.

6.23.4 Evidence into recommendations

In developing the recommendation for this section the guideline the GDG also took into account the reviews of family members experience in Chapter 4 of this guideline which confirmed the view that families typically have considerable unmet needs. This meant that despite the limited evidence that the GHDG felt that the provision of information and the use of a range of self-help intervention (with relatively low cost) should be offered to families. The GDG also felt that were families could not make use of or have not benefitted from the use of the self-help materials that an offer a structured intervention as set out in the 5-Step intervention should be made.

6.23.5 Recommendations

6.23.5.1 When the needs of families and carers of people who misuse alcohol have been identified:

- offer guided self-help, typically consisting of a single session, with the provision of written materials
- provide information about, and facilitate contact with, support groups (such as self-help groups specifically focused on addressing the needs of families and carers).

6.23.5.2 If the families and carers of people who misuse alcohol have not benefited, or are not likely to benefit, from guided self-help and/or support groups and continue to have significant problems, consider offering individual family meetings. These should:

- provide information and education about alcohol misuse
- help to identify sources of stress related to alcohol misuse
- explore and promote effective coping behaviours
- typically consist of at least five weekly sessions.

6.24 Children and young people

6.24.1 Introduction

While drinking and alcohol use disorders are relatively rare under the age of 10, the prevalence increases steeply from the teens to peak in the early twenties. The United Kingdom has the highest rate of underage drinking in Western Europe (Hibbell et al., 2010). This is of particular concern as alcohol presents particularly serious consequences in young people due to a higher level of vulnerability to the adverse effects of alcohol. Heavy drinking in adolescence can affect brain development and has a higher risk of organ damage in the developing body (Brown et al., 2008).

The number of adolescents consuming alcohol has decreased to 54% between 1988 and 2007 but the amount consumed by those drinking doubled over the same period to 12.7 units per week.(Fuller, 2008) Regular alcohol consumption in adolescence is associated with increased accidents, risky behaviour including unprotected sex, antisocial behaviour, violence and decreased family, social and educational functioning. There is evidence of an association between hazardous alcohol consumption in adolescence and increased level of alcohol dependence in early and later adulthood (Hingson et al., 2006). For example, alcohol consumption before the age of 13 is associated with a fourfold increased risk of alcohol dependence in adulthood. Adolescents with early signs of alcohol misuse who are not seeking treatment are a critical group to target interventions towards. Adolescent alcohol related attendances at accident and emergency departments saw a tenfold increase in the United Kingdom since 1990 and a recent audit estimates 65,000 alcohol-related adolescent attendances occur annually.

Comorbid psychiatric disorders are considered to be 'the rule, not the exception' for young people with alcohol use disorders. (Perepletchikova et al., 2008). Data from the National Comorbidity study demonstrated that the majority of lifetime disorders in their sample were comorbid disorders (Kessler 1996). This common occurrence of alcohol use disorders and other substance use disorders along with other psychiatric disorders notes the importance of a comprehensive assessment and management of all disorders. Disruptive behaviours disorders are the most common comorbid psychiatric disorders among young people with substance use disorder. Those with conduct disorder and substance use disorder are more difficult to treated, a higher treatment drop-out rate, and have a worse prognosis. This strong association between conduct disorder and substance use disorder is considered to be reciprocal, with each exacerbating the expression of the other. Conduct disorder usually precedes or coincides with the onset of substance use disorder, with conduct disorder severity found to predict substance use severity. Significantly higher rates of ADHD has been reported in those young people with substance use disorders, data from untreated adults with ADHD indicate a higher risk of developing substance use disorders and at an earlier age compared to treated controls. Those with ADHD have a more prolonged course. However, those young people with ADHD and co-occuring conduct disorder or bipolar disorders are at highest risk of development of substance use disorders. High rates of depression and anxiety have been reported in adolescents with alcohol use disorders, with increased rates of suicidality. Among clinical populations for substance use disorders, there was an increased rate of anxiety symptoms and disorder, post traumatic stress disorder and social phobias (Clark et al., 1997). For young people the

presentation may be different as dependence is not common, with binge drinking more the pattern seen, this often alongside poly drug use. Criminality and offending behaviour are often closely related to alcohol misuse in children and adolescents. Liaison with criminal justice services is necessary to ensure appropriate co-ordination of care and effective communication and information sharing protocols are in place.

In addition to the problems presented by comorbid disorders, the concept of dependence and criteria for diagnosis (DSM-IV or ICD 10) has limitations when applied to adolescents, this because of the low prevalence of withdrawal symptoms, and the low specificity of tolerance in this age group (Chung et al., 2001) . The adolescent therefore may continue drinking despite problems, problems being manifest as difficulties with school attendance, co-morbid behavioural difficulties, arguments at home, and peer affiliation.

As has been noted previously relationships with parents, carers and the children in their care are often damaged by alcohol misuse (Copello et al., 2005). The prevalence of alcohol use disorders in the victims and perpetrators of domestic violence provides an importance rationale for the exploration of these issues. Sexual abuse has been found to be prevalent in alcohol dependent drinkers seeking treatment and may be a particular concern with young people with alcohol abuse problems. (Moncrieff & Farmer, 1998; Moncrieff et al., 1996). For young people both their own alcohol misuse and that of their parents or carers may be a safeguarding concern. The Children Act (2004) places a statutory duty on services providing assessments to make arrangements to ensure that their functions are discharged having regard to the need to safeguard and promote the welfare of children. Services that are involved with those who misuse alcohol fit into a wider context of safeguarding young people from harm and need to work to ensure that the rights of children, young people and their parents are respected. Local protocols between alcohol treatment services and local safeguarding and family services determine the specific actions to be taken (HM Government, 2006; DCSF, NTA & DH, 2009).

6.24.2 Current service provision

In the UK, most of treatment is community based and provided as part of the range of services and models. These can be services provided by CAMHS in Tier 2 and 3 services, specific CAMHS addiction services and other commissioned specialist services that are formed by a range of practitioners, generally Tier 2/3 working together from the youth offending teams, the looked after teams and voluntary sector. Much of the focus is on engagement, health promotion and retention in services. In addition, in the UK, services which offer treatment tend to prioritise drug misuse such as opiate and cannabis misuse and not alcohol. Given the comorbidity noted above many adolescents who are in receipt of treatment for alcohol treatment are often treated in specialist services such as Youth Offending Teams or specialist services for young people with conduct disorders such as the new developed multisystemic therapy teams (DH, 2007), though identification and treatment of their dependence and/or harmful use may not be fully explored. In the US, adolescents with substance use disorders receive treatment in a variety of settings, community, residential, criminal justice settings, and home based treatment. However, there is little research evaluating the differences between these setting. As a consequence this is little clear evidence to determine the most appropriate treatment environments. The American Academy of Child and Adolescent Psychiatry, (2001)

recommend that factors affecting the choice of setting should include: the need to provide a safe environment, motivation of the adolescent and his/her family to cooperate with treatment; the need for structure and limit-setting; the presence of additional medical or psychiatric conditions and risk associated; availability of specific types of treatment settings for adolescents; preferences for treatment in a particular setting; and treatment failure in a less restrictive/intensive setting in the past.

6.25 The assessment of harmful alcohol use and dependence in children and young people

6.25.1 Introduction

A number of instruments that aid in the identification and diagnosis of alcohol misuse in children and young people are available. In considering the development of the assessment tools for children and young people, the GDG considered the framework set out within the Models of Care for Alcohol Misusers (NTA, 2006), but felt that the service structures for children and adolescent services, the nature of the problems presented by children, and the need for an integrated treatment approach with child and adolescence services, meant that this service model needed significant modification. After consideration, the GDG decided to concentrate on two key areas for assessment tools:

1) A case identification/diagnostic assessment
2) A comprehensive assessment.

The remainder of this review is therefore structured around these two areas. The clinical questions set out below relate specifically to these two areas.

6.25.2 Clinical Questions

The clinical questions which the GDG addressed, and from which the literature searches were developed were:

d) What are the most effective a) diagnostic and b) assessment tools for alcohol dependence and harmful alcohol use in children and young people (aged 10-18 years)?

e) What are the most effective ways of monitoring clinical progress in alcohol dependence and harmful alcohol use in children and young people (aged 10-18 years)??

6.25.3 Definition and aim of review of diagnostic and assessment tools for alcohol dependence and harmful alcohol use

This section was developed in conjunction with the review of assessment tools and the structure and format for the delivery assessment for alcohol services for adults in Chapter 5. The strategy for identifying potential tools was the same as adopted for adults. See Chapter 5 for databases searched and clinical review protocol, and procedure for evaluating assessment tools for inclusion in diagnostic accuracy meta-analyses.

As was the case with the review of adult assessment tools, the original intention was to conduct a quantitative review assessing the sensitivity, specificity and positive predictive value of the instruments for case identification, diagnosis, assessment and alcohol related problems in children and young people. However, the search failed to identify sufficient data to allow for a quantitative review. As a result, a narrative synthesis of the tools was undertaken and the conclusions are presented below. The identification and subsequent criteria necessary for inclusion in the narrative review of assessment tools were that the tool assesses primarily alcohol and not drugs; the tool has either been developed for use in children and young people or has been validated in this population; the tool has established and satisfactory psychometric data (e.g. validity/reliability and sensitivity/specificity); the tool assesses a wide range of problem domains (e.g. dependence, quantity/frequency of alcohol consumed, alcohol-related problems etc.); and the tool has favorable administrative properties (e.g. copyright, cost, time to administer etc.).

6.25.4 Narrative synthesis of assessment tools for children and young people

Case identification/diagnosis

Three assessment tools for case identification were initially identified as assessed for the properties outlined above. From the review of the literature using the stipulated inclusion and exclusion criteria, the GDG identified three tools for case identification in children and young people. These were the Adolescent Alcohol Involvement Scale (AAIS; Mayer & Filstead, 1979), the Adolescent Drinking Index (ADI; Harrell *et al.,* 1985), and the Alcohol Use Disorders Identification Test (AUDIT; Babor *et al*., 2001). Both the AAIS and ADI have both been developed for use in an adolescent population. However, the AAIS has not been adequately validated, and the ADI although claiming adequate reliability and validity data, is not routinely used in the UK. As was the case in the review of adult assessment tools in Chapter 5, the AUDIT questionnaire, was deemed as the most appropriate and suitable for use as a case identification/diagnostic instrument. For a review of the psychometric properties and characteristics of the AUDIT, see chapter 5. We also reviewed which investigated the need for revised cut off in adolescents using the AUDIT questionnaire. Chung *et al.,* (2002) also recommend modification of the AUDIT to be more appropriate to adolescents. Two studies using representative populations suggest a cut off score of 4 or more (Chung *et al.,* 2002; Santis *et al.*, 2009).

Comprehensive assessment instruments

As part of the systematic review and associated search strategies, a number of clinical interview tools which provide a comprehensive assessment of alcohol misuse in children and young people specifically were identified. These are: the Adolescent Diagnostic Interview (ADI; Winters & Henly, 1993); the Comprehensive Addiction Severity Inventory for Adolescents (CASI-A; Meyers *et al.,* 1995); the Customary Drinking and Drug Record Use (CDDR; Brown *et al.*, 1998); the Diagnostic Interview Schedule for Children (DISC; Piacentini *et al.,* 1993); the Structured Clinical Interview for the DSM Substance Use Disorders Module (SCID SUDM; Martin *et al.,* 1995); the Substance Use Disorders Diagnostic Schedule (SUDDS-IV; Hoffman & Harrison, 1995); and the Teen Addiction Severity Index (T-ASI; Kaminer *et al.,* 1991). Based on

the criteria outlined above, the clinical interview tools which met inclusion criteria and are included in this narrative review are the ADI, DISC and T-ASI (see table 1 below for characteristics of these tools). The group made a consensus-based decision to exclude the CASI-A, CDDR, SCID SUDM, and SUDDS-IV from the narrative review as these tools have been developed for the use in adolescents over the age of 16 years old population only and hence may be inappropriate for use with children under that age. See Table 57 for characteristics of these excluded tools.

The Adolescent Diagnostic Interview (ADI) is a comprehensive assessment instrument which provides a DSM-III-R based psychiatric diagnosis of alcohol abuse or dependence in 12 to 18 year olds. As well as substance and alcohol abuse/dependence, the ADI also assesses a variety of other problems such as psychosocial stressors, cognitive impairment and school and interpersonal functioning. The ADI as a clinical instrument has been reported to have good inter-rater reliability (alcohol abuse = 0.86; alcohol dependence = 0.53); test-retest reliability (0.83); significant concurrent validity among all variables (range = .58-.75); adequate criterion validity assessed by agreement with a clinician rating (alcohol abuse k=0.71; alcohol dependence k=0.82); and high sensitivity and specificity for alcohol abuse (both 0.87) and dependence (0.90 and 0.95 respectively) (Winters *et al.,* 1993; 1999). The ADI takes 50 minutes to complete and can be obtained at a cost from the developer.

The Diagnostic Interview Schedule for Children (DISC) provides a diagnosis of alcohol dependence or abuse based on DSM-IV criteria. It has been found to be highly sensitive in identifying young people who have previously been diagnosed as having a substance use disorder (sensitivity = 75%) (Fisher *et al.,* 1993). However, although the DISC has been found to have acceptable reliability and validity data, this has been for non-substance specific psychiatric disorders (see Schwab-Stone *et al.,* 1995; Piacentini *et al.,* 1992; Schaffer *et al.,* 1995; Jensen *et al.,* 1995). It is also relatively lengthy (1-2 hours), and copyrighted.

The Teen Addiction Severity Index (T-ASI) is a semi-structured clinical interview designed to provide a reliable and valid measure in the evaluation of substance abuse in adolescents. It has 126 items which provides severity ratings for psychoactive substance use, school or employment status, family function, peer-social relationships, legal status and psychiatric status. The T-ASI has satisfactory inter-rater reliability (r= 0.78) and has been found to have utility in both the clinical identification of alcohol dependence or harmful alcohol use, as well as in the assessment of changes of severity over time as a response to treatment and hence may be applicable as an outcome monitoring tool (Kaminer *et al.,* 1991). Kaminer *et al.,* (1993) also established that the T-ASI could adequately distinguish between 12-17 year old with and without substance use disorders as defined by the DSM-III-R. The T-ASI has an added benefit as it can be administered in less than 30 minutes, it is free to use and not copyrighted.

No measures of alcohol problems, such as the APQ for adults, was identified and nor was any specific instrument, such as the RCQ-TV for motivation, identified (See Chapter 5).

Table 86. Characteristics of clinical interview tools included in narrative review

Assessment Instrument	Number of Items & Format	Time to administer & by Whom

		Training required for administration, Time to Score, By Whom
Adolescent Diagnostic Interview (ADI)	213 items (not all asked), structured interview	Approx 50 minutes (depends on number of substances used), trained personnel Yes, 15-20 minutes, trained personnel
Diagnostic Interview Schedule for Children (DISC)	Variable depending on module assessed, structured interview Scoring algorithms are provided by NIMH-DISC	1-2 hours, trained personnel No, Immediate, computer program
Teen Addiction Severity Index (T–ASI)	154 (7 subscales), structured interview	20-45 mins, trained personnel Yes, 10 minutes, non-trained personnel

A framework for assessment for child and young people with alcohol problems

As with the adult assessment, the use of any assessment tool needs to be set in context. The context here is that all children who are beyond initial identification should be offered an assessment within specialist child and adolescent mental health services. Although recommendations are made below for the use of specific measures to assess the nature and extent of the alcohol misuse and related problems, it was also the view of the GDG that the assessment should take place in the context of a comprehensive overall assessment of the mental health, educational, and social care needs of the children and young people, in line with current best practice (DfES, 2007). In common with good assessment practice in CAMHS Services the involvement of parents, carers, and others (e.g. schools) is an essential part of any assessment. It should also be noted that parents not only have a key role as informants, advisors and participants in the process of assessment, but they also have a key role to play in the development of any future treatment plans. It is therefore important that wherever possible they are involved from the beginning.

The overall structure of assessment (at least for the assessment of alcohol misuse) is provided, by the assessment tools reviewed above. However, whatever assessment tool is used both from the child and adult literature, (Harrington *et al.,* 1999 and see Chapter 5) suggest that the following domains need to be considered as part of any assessment of alcohol related problems in children and young people:

- Alcohol use – consumption, dependence features and associated problems
- Co-morbid substance misuse– consumption, dependence features and associated problems
- Motivation
- Self efficacy
- Other problem domains
    - Physical history and problems

    - Mental health and problems
    - Social functioning
    - Educational attainment and attendance
    - Peer relationships
    - History of abuse and trauma
    - Family functioning and relationships
- Risk assessment
- Developmental needs of the young person
- Treatment goals
- Obtaining consent to treatment
- Formulation of a care plan and risk management plan

Additional points to bear in mind, is the use of further informants. For example, in terms of the assessment of consumption, the use of other informants such as parents, carers or schools may assist in detailing the history of consumption and clarifying the level and veracity of use. As was identified in the Introduction, the presentation of alcohol misuse or dependence does not typically follow the pattern seen in adults. More often, a pattern of binge drinking is observed often accompanied by drug misuse. It is important, therefore, to detail this both the pattern of drinking and the comorbid drug misuse. It should also be noted that adolescents may have lower prevalence of withdrawal symptoms along with a lower tolerance. Both these factors may contribute to continued high alcohol intake, particularly of binge drinking, with consequent serious implications for psychological and physical health, but without the 'warning signs' of emerging withdrawal symptoms.

Use of biological markers

The review of adult alcohol misuse identified that no particular biological markers were of value in achieving a diagnosis of harmful or dependent drinking. Given that clinically significant changes in liver enzymes are rare in adults, even with established alcohol dependence (Clarke *et al.,* 2001)), it seems unlikely that the routine use of such biological markers is of value in adolescents. However, the use of urine analysis or breath testing to determine the presence during treatment and/or assessment of drug or alcohol misuse, maybe of value in assessing the veracity in the overall assessment, but should not be used as a diagnostic marker.

History of trauma and abuse

It has already been noted that comorbidity of substance misuse is significantly higher in adolescents who misuse alcohol. It is also important to note that alcohol misusing adolescents have a significant increased rate of physical abuse (by a factor of 6-12) and a significant increased rate of sexual abuse (by up to a factor of 20) (Clark *et al.,* 1997). Given that it is

possible that these histories may have a significant etiological role in the development of alcohol misuse, it is important that these issues are part of assessment. It is also likely that a history of trauma has an impact for the likely comorbidity, for example, the existence of PTSD (Clark, *et al.*, 2003) and also that it may be associated with poor response to treatment and the need for more complex treatment interventions.

6.25.5 Evidence Summary

The GDG identified that the AUDIT is appropriate for case identification of alcohol misuse in children and young people but with the proviso that the cut-offs are adjusted downwards to a score of 4 or more. Also modification of AUDIT items to be relevant to adolescents should be considered. The advantages identified for adults, that is brief, easy to administer and score remain the same.

The review of tools to aid a comprehensive assessment in children and young people identified three possible tools, the ADI, the DISC and the T-ASI. The review identified some problems with the DISC including population non which it was standardised, its duration and its cost. The other two instruments (the ADI and the T-ASI) met the criteria chosen by the GDG and therefore both could be used as part of a comprehensive assessment of alcohol misuse. However, although the T-ASI is free to use, the ADI can only be obtained at a monetary cost. Furthermore, the T-ASI has utility as an outcome monitoring tool and although perhaps too long for routine use (30 minutes) it may have value as an outcome measure for periodic reviews. As with the adult assessment, these tools should be used and interpreted by trained staff. The comprehensive interview should not only assess the presence of an alcohol use disorder, but also other comorbid and social problems, development needs, educational and social progress, motivation and self-efficacy and, risk. Consent for assessment and treatment must be obtained from the child and their guardian. The aim of the assessment should be, wherever possible to set a treatment goal of abstinence.

6.25.6 Assisted alcohol withdrawal assessment and management

As has already been noted, the diagnosis and identification of withdrawal symptoms in children and young people is difficult. This means that the potential for harm through under-identification of alcohol withdrawal on young people is considerable. Unfortunately, there is little direct evidence to guide the process of withdrawal management, including both its identification and treatment in young people. In the development of this section the GDG drew extensively on the review of assisted withdrawal for adults, contained both in the NICE guideline for acute withdrawal (NICE, 2010b) and for planned withdrawal within this guideline. In essence, the data therefore, used to support much of this review is an extrapolation from a data set developed from the management of withdrawal in adults. The principle that the GDG approached this data with is one of considerable caution and a desire to, as far as possible, reduce any significant harm arising from withdrawal symptoms in young people.

Identification of need for assisted alcohol withdrawal

Identification of withdrawal should be based on careful assessment of the pattern, frequency and intensity of drinking. The limited data available for review, the evidence from adults and the greater vulnerability of young people to the harmful effects of alcohol led the GDG to

conclude that they should be a significant reduction in the threshold for young people for initiating withdrawal management. The threshold that has been established for adults of an AUDIT score > 20, an SADQ score of >20 or the typical consumption of 15 units per day is not appropriate for adolescents. In adolescents binge drinking is common (defined as more that 5 units of alcohol on any one occasion) and a pattern of frequent binge drinking (for example, a pattern of two or more episodes of binge drinking in a month) or an AUDIT score 15 should alert the clinician to possible dependence and trigger a comprehensive assessment. The presence of any potential withdrawal symptoms should be taken seriously and a comprehensive assessment initiated. A range of factors including age, weight, and previous history of alcohol abuse and the presence of co-occurring disorders will also influence the threshold for initiating a comprehensive assessment and withdrawal management. Given the uncertainty about the severity of withdrawal symptoms and the potential negative consequences for children and young people of withdrawal, the GDG also felt that it was prudent to recommend that all assisted withdrawal for children and young people take place in an acute inpatient or residential setting with significant medical and nursing staff availability on a 24 hour basis.

Drug regimens in assisted withdrawal

The use of the same drug regimens as for adults, doses appropriately adjusted for age and alcohol usage should be used. The evidence for favouring either symptom triggered or fixed dose regimens with children and young people remains uncertain as there are no trials which have investigated this issue. Nevertheless whichever regimen is chosen there is a clear requirement for very close monitoring of withdrawal symptoms. Given the uncertainty identified in this guideline about the capacity of staff to manage symptom triggered withdrawal, where symptoms are easily identifiable, it was suggested that the cautious approach to the management of symptoms in young people is a fixed dose regimen but with very close symptom monitoring using a validated rating scale such as the CIWA-Ar.

6.25.7 Evidence Summary

There is little evidence which indicates the identification and treatment practices needed for assisted withdrawal in children and young people. Therefore, the GDG makes a consensus-based decision to extrapolate from the review of the adult literature and combine this with expert opinion. The group concluded that a comprehensive assessment and possible assisted withdrawal should be offered to all children and young people with an established drinking of binge drinking, an AUDIT score >15 and this who consume above 5 units per day but this decision should also take into consideration other factors such as age, weight, previous history of alcohol abuse and the presence of co-occurring disorders. There is no direct evidence that suggests added benefit of a symptom-triggered regimen over a fixed-dosing regimen. However, as the GDG recommend that all assisted withdrawal for children and young people should take place in an inpatient setting which should have continuous monitoring and care, a symptom-triggered approach should be considered.

6.26 Treatment interventions to reduce harmful drinking, promote abstinence and prevent relapse in children and young people with harmful drinking and alcohol dependence

In the development of the adult treatments sections of this guideline it was accepted for some people who misuse alcohol (in particular those with harmful use or mild dependence) the reduction in alcohol consumption might be an option. However, given the potential long-term harm suffered by children and young people with harmful drinking and alcohol dependence and the frequent presence of comorbid substance misuse and other psychiatric disorders, it is felt that the appropriate goal for children and young people should be achieving abstinence. However, it was recognised by the GDG that considerable difficulties are faced by some young people in trying to achieve abstinence and particularly if the support they receive from their families, carers and others in limited or non existent or they experience considerable peer pressure to drink alcohol. Therefore, for some young people the GDG accepted that that an initial reduction in alcohol misuse maybe the only achievable short-term objective. Nevertheless, the GDG's view was that given the considerable problems that young people face, that abstinence remained the preferred goal.

A further important difference between the treatment of adults and young people concerns the presence of comorbidities. Although comorbid depressive and anxiety symptoms are common in adults with harmful drinking and alcohol misuse (Weaver *et al.,* 2007), the extent and severity of the comorbidities often found in children is greater (Perepletchikova *et al.,* 2008). Comorbid disorders such as conduct disorder and attention deficit and hyperactivity disorder significantly complicate the management alcohol misuse and concurrent treatment of them is to be considered. This problem is well known (Perepletchikova *et al.,* 2008) and a number of treatments, for example, multi-systemic therapy (Henggeler *et al*., 1999) , or treatment such as brief strategic family therapy (Szapocznik *et al*., 2003 or multi-dimensional family therapy (Liddle *et al.,* 1992) have been developed for conduct disorder explicitly to deal with the complexity of problems faced by children and young people including drug and alcohol misuse. The later two interventions have a very explicit focus on substance misuse. At the heart of all these interventions, lies the recognition of the considerable complexity of problems presented by young people with alcohol and drug misuse and the need often to develop a multi-systems, multi-level approach to deliver an integrated approach to treatment.

6.26.1 Review of psychological interventions

This section aims to review the evidence for psychological interventions for the treatment of alcohol dependence and harmful alcohol use in children and young people. However, although there are several published reviews on the efficacy of psychological interventions for adults and for the prevention of adolescent substance misuse, there are only a limited number of trials assessing the clinical efficacy of psychological interventions for alcohol misuse alone (without comorbid drug abuse) for children and young people under the age of 18 years old. In addition, the patient populations assessed in these trials more often than not have comorbid substance

misuse. Therefore, a GDG consensus-based decision was agreed that the literature search would be for alcohol-specific primary studies as well as published systematic reviews to guide the overall strategy of a narrative synthesis of the evidence.

Psychological therapies were considered for inclusion in the review if they were:-

- Alcohol-focused only
- Planned treatment (especially for brief interventions)
- For treatment-seeking participants only (of particular importance for the brief interventions as our scope did not cover opportunistic brief interventions – see scope Appendix 1)
- Manual-based or in the absence of a formal manual, the intervention should be well-defined and structured
- Ethical and safe

6.26.2 Clinical Questions

Primary clinical question addressed in this section is:
For children and young people with alcohol dependence or harmful alcohol use is *treatment x* when compared to *y* more clinically and cost-effective and does this depend on the presence of comorbidities?

6.26.3 Clinical review protocol

Table 87. Clinical review protocol for the review of psychological therapies for children and young people.

Electronic databases	CENTRAL, CINAHL, EMBASE, MEDLINE, PSYCINFO
Date searched	Database inception to March 2010
Study design	RCT (≥ 10 participants per arm); Systematic reviews
Patient population	Children and young people (10 – 18 years) At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week
Interventions	Individual or group interventions; multi-component interventions
Comparator	Control or other active intervention
Critical Outcomes	Abstinence Amount of alcohol consumed Rates of Consumption Relapse (> X number of drinks or number of participants who have relapsed) Lapse (time to first drink or number of participants who have lapsed) Attrition (leaving the study early for any reason)

As part of the overall search for effective individual, group and multi-component psychosocial interventions for children and young people, the review team conducted a systematic review of published systematic reviews (in part to take account of the complex comorbidity) of interventions for young people with drug and alcohol misuse and also randomised controlled trial of psycho-social interventions for children and young people specifically alcohol misuse was conducted. The literature search identified a number of primary studies investigating the efficacy of psychological therapies for children and young people. However, the participant

population in these studies did not reach inclusion criteria for drinking severity and could not be classified dependent/harmful.

6.26.4 Studies included in narrative synthesis

This review of the effective psychosocial interventions for children and young people should be read in conjunction with the review of brief interventions contained in the NICE public health guidance (NICE, 2010a), and the review of psychological interventions for adults contained in within this guideline. A limited number of studies, specifically on alcohol focused interventions, have been undertaken for children and young people. However, a number of studies have considered the treatment of conduct disorder in the presence of drug or alcohol misuse. In light of this significant comorbidity, in addition to the two guidelines referred to above, the GDG also drew on other recent NICE guidelines, specifically the review of conduct disorders for adolescents contained within the NICE guideline on Antisocial Personality Disorder (NICE 2008) and three other systematic reviews (Waldron and Kaminer (2004); Perepletchikova *et al.*, 2008; Tripodi *et al.,* 2010). Individual and group based therapies and multi-component interventions used in the treatment of alcohol dependence and harmful alcohol use in children and young people were considered in the review of the evidence.

Individual and group psychological interventions

The public health guidelines on the prevention of alcohol related problems in adults and young people (NICE 2010a) and also the NICE public health guidance on community interventions for vulnerable young adults (NICE, 2007) , recognise the value of individual and/or group CBT. A number of studies which assess the use of individual or group based psychological therapies have been identified and reviewed Waldron and Kaminer (2004); Perepletchikova *et al.,* 2008; and Tripodi *et al.,* 2010).

In a recent systematic review, Tripoldi *et al.* (2010) conducted a meta-analysis of experimental studies (including RCTs) evaluating both individual/group based interventions collectively (brief interventions, MET and CBT) as well as family-based therapies with a focus on reducing alcohol abuse. However, of these studies, only a limited number of trials evaluated the use of CBT (with an emphasis on relapse prevention) and MET in a sample of children or young people identified with harmful or dependent drinking (the specific focal point of this guideline. The review consisted of 16 studies (14 RCTs, 2 were quasi-experimental) assessing both individual/group treatment and multi-component therapies. Ten of these included studies assessed individual/group treatment. However, of these studies included in the meta-analysis, the main issues encountered were in the studies were that they are concerned with individuals who did not meet criteria for harmful drinking or alcohol dependence (n=1), were with a participant population with a significant comorbidity with psychiatric disorder (n=2) and in the majority of cases, the focus was not specifically on alcohol misuse, but rather on substance misuse more generally (n=7). The results of this meta-analyses showed a significantly large effect in drinking reduction for individual interventions (Effect Size = -0.75; 95% CI, -1.10 to -0.40) However, the meta-analyses did not distinguish between different types of individual interventions in pooled analyses therefore other reviews which focused on specific interventions were considered.

Brief Interventions and Motivational Interviewing

Both the NICE prevention of alcohol related problems in adults and young people (NICE 2010a) and also the NICE public health guidance on community interventions for vulnerable young adults consider the evidence for brief motivational techniques (motivational interviewing and motivational enhancing techniques). Motivational interviewing and other brief interventions may serve to heighten motivation, increase self-efficacy, and provide personalized feedback and education tailored to specific substances and comorbid problems such as psychiatric disorders. The evidence for is mainly from the adult literature though there is an emerging literature for adolescents where modifications of motivational interviewing or enhancement techniques for adolescents have shown promise for both evaluation and treatment based on limited treatment studies (Colby *et al.,* 1998; Monti *et al.,* 1999). However, a more recent review Perepletchikova *et al.* (2008) reported uncertain outcomes for MET when used alone with alcohol use disorders (Note this is consistent with the approach to harmful and dependent alcohol misuse identified for adults in this guideline). There is some evidence to suggest that motivational techniques when combined with CBT may be effective, for example in the Cannabis Youth Trial (CYT; Dennis *et al.,* 2004), although this population were predominately diagnosed as dependent on cannabis.

Cognitive Behavioural Therapy (CBT)

Waldron and Kaminer (2004) in a review of CBT approaches to substance use disorders (more broad than just alcohol misuse) concluded that individual CBT treatment may be effective in reducing substance misuse as well as other related problems. They also made a number of suggestions about the adaptation of CBT approaches to young people, addressing developmental stages and levels of maturity. In their review they also reported that CBT in group format to be as effective as individual therapy. For example, CBT has been applied both in individual and group modalities in combination with family approaches and MET. Interventions with the adolescent alone (e.g. CBT or CBT plus have been reported as effective (Dennis *et al.,* 2004; Kaminer and Burleson, 1999; Kaminer *et al.,* 1998). However, much of the evidence base is from approaches dealing with comorbidity such as conduct disorders, and anxiety and affective disorders and where information on the extent and severity of alcohol misuse specifically is lacking. Perepletchikova *et al.* (2008) in a subsequent review considered 5 studies looking at the effectiveness of CBT in the reduction of alcohol use disorders, three of which were of CBT alone, one evaluated an integrated family and group CBT approach and one looked at efficacy of CBT on reduction of substance use in those with comorbid conduct disorder again it appears that the data is primary concerned with children and young people who did not have ht severity of alcohol misuse that is the primary focus of the guideline.

Kaminer *et al.* (2002) in one of the few studies that had a more substantial proportion of participants with alcohol dependence randomised significant to CBT or a psychoeducational therapy reported on reductions across both therapies. Of 88 subjects, 12.5% had an alcohol use disorder only. However, of the 64 subjects having an alcohol use disorder, 58% met criteria for abuse and 42% for dependence. At three months alcohol use had improved significantly and to 9 months showed continued improvement. Substance use also showed a positive trend towards improvement. Kaminer *et al.* (2008) only included participants who meet DSM-IV criteria for alcohol dependence, although 81.8% of the sample also used marijuana. However, all participants received CBT and the focus on the study was on aftercare.

Although the primary focus of comorbidity has been on individuals with conduct disorder, a few studies have also examined the problems presented by co-occurring common mental health disorders, such as depression and anxiety. One study evaluated the efficacy of an integrated 20-week programme of CBT with case management in an a population of substance abusing young people (aged between 15 and 25 years). Sixty-three percent of the sample met criteria for alcohol dependence. Treatment resulted in a significant improvement in abstinence rates as well as a reduction in the number or participants meeting diagnostic thresholds for dependence. These positive effects were also observed at 44 week follow-up. This study (like others) evaluates the effectiveness of psychological interventions for young people include participants whom are over the age of 18 years. However, this age-range makes interpretation of data sets such as this difficult.

Twelve Step Facilitation (TSF)

The development of Twelve Steps Facilitation (TSF), which grew out of the initial work of Alcohol Anonymous has been developed in to a treatment intervention for adults (Project Match, 1993;1997) has not been tested as an individual treatment in adolescents with harmful and dependent drinking. There have been no programmes for adolescents built around the 12 step model, and as far as the GDG were aware (or were able to identify), no evaluation of the effectiveness of a 12-step model for children and young people. It should be noted that some residential treatment centres for adolescents have been developed on refinement TSF resulting in the development of residential treatment models, e.g. the Minnesota model (Winters *et a.l,* 2000) but no formal evaluations in alcohol dependent adolescents were identified.

6.26.5 Evidence summary

The evidence reviewed using these systematic reviews and primary studies suggests that although there has been recent progress in the development of individual or group psychological treatment of alcohol dependence and harmful alcohol use in children and young people no individual treatment has a convincing evidence base for harmful use of dependence. In some respect this finding is in line with the adult literature and findings of our own meta-analyses where a number of structured treatments including CBT, behaviour therapy and social network behaviour therapy had some benefits for harmful and mildly dependent drinkers (see section 7) but it was not possible to distinguish between them. The issue is further complicated by the fact that many of the trials evaluating the efficacy of these intervention, and representative of this population, involved participants with comorbid substance misuse.

6.26.6 Multi-component psychological interventions

Components of a multi-component intervention

The need to involve family members, particularly parents has been recommended in policy guidance eg. *Every Parent Matters* (DfES, 2007) and in *Supporting and Involving Carers* (NTA, 2008). This involvement is multi-fold: to obtain (depending on consent of the child and capacity) any necessary consent to treatment, to engage the support of the family in the treatment

process, to obtain more information on the assessment of the child's alcohol use and general functioning, ascertain possible involvement in parent training, coping skills and problem solving approaches to parenting, and more formal involvement in specific family programmes. Family involvement has been shown to be positively associated with improved outcomes on domains and level of engagement of the young person (Dakof *et al.,* 2001).

Common elements identified for review in these programmes include comprehensive assessment and monitoring, a focus on engagement of individuals, and usually their families, in treatment explicit linking of goals and interventions at all levels of the system. A goal focused approach to treatment of family substance abuse, the involvement of the family aimed at improving family communication problem solving and parenting skills, and the provision of individual interventions, again often focused on coping skills identified for the child or young person. The programmes also require staff who are experienced and highly trained clinicians (all were graduates, most had masters or doctoral degrees).

Although there are many approaches to family intervention for substance abuse treatment, they have common goals: providing education about alcohol and drug misuse, improve motivation and engagement; assisting in achieving and maintaining abstinence; setting consistent boundaries and structure; improving communication, and providing support. Family interventions are the most evaluated modality in the treatment of adolescents with substance use disorders. Among the forms of family based interventions are functional family therapy (Alexander *et al.,* 1990); brief strategic family therapy (Szapocznik *et al.,* 1988), multisystemic therapy (Henggeler *et al.,* 1992) and multidimensional family therapy (Liddle *et al.,* 1992). An integrated behavioural and family therapy model that combines a family systems model and CBT has also been developed (Waldron *et al.,* 2001).These interventions fall broadly under what would be called a systemic approach. They do not focus explicitly on the provision of specified individual interventions but rather it is for the therapist, in conjunction with their supervisor, to develop the specific therapeutic approach in light of the identified needs of the young person. Some trials, such as the large trial of cannabis abuse and dependence (Dennis *et al.,* 2004), have focused on the provision of a systemic approach (in this case MDFT) but have also provided a specified range of psychological interventions such as MET, the development of a family support network including parental education, the development of conditioning models from children in the community.

Definitions of interventions

Functional family therapy is a psychological intervention that is behavioural in focus. The main elements of the intervention include engagement and motivation of the family in treatment, problem-solving and behaviour change through parent training and communication training, and seeking to generalise change from specific behaviours to have an impact on interactions both within the family and with community agencies such as schools (see for example Gordon *et al.*, 1995).

Brief strategic family therapy is a psychological intervention that is systemic in focus and is influenced by other approaches such as structural family therapy. The main elements of this intervention include engaging and supporting the family, identifying maladaptive family

interactions and seeking to promote new more adaptive family interactions (see for example, Szapocznik *et al.*, 1989).

Multi-systematic therapy involved using strategies from family therapy and behaviour therapy to intervene directly in systems and processes related to antisocial behaviour (for example, parental discipline, family affective relations, peer associations, and school performances) for children or adolescents (Henggeler *et al.*, 1992).

Effectiveness of multi-component interventions

The GDG used the NICE ASPD guideline (NICE, 2009) review of family interventions and multi-systematic therapies for the treatment of conduct disorder This guideline used the definitions above. The primary focus of their review was on reduction in offending behaviour but all the interventions, in particular BSFT and MDFT, had an explicit focus on substance misuse.

In the ASPD guideline, the meta-analysis of 11 trials assessed the effectiveness of family interventions. The results of the meta-analysis showed that family interventions are more effective than control for reducing both behavioural problems (SMD -0.75; -1.19 to -0.30) and offending (RR -0.67; 0.42 to 1.07). Furthermore, 10 trials on multisystemic therapy that met the inclusion criteria for the review were analyses. There was significant heterogeneity for most outcomes; however, there was consistent evidence of a medium effect on reduction in offending outcomes including number of arrests (SMD -0.44; -0.82 to -0.06) and being arrested (RR 0.65; 0.42 to 1.00).

In a recent meta-analysis, Tripoldi *et al.,* (2010) six trials evaluating multi-component and family-based interventions were included in the systematic review. However, all of these trials were not focused specifically on alcohol misuse, and in two of the trials, only approximately 50% of the sample met criteria for alcohol dependence and harmful alcohol use. The overall findings were in line with the NICE ASPD guideline (NICE, 2009) the review did however report that that multi-component family therapies were effective in reducing drinking in adolescents (Hedges g = -0.46, 95% CI, -0.66 to -0.26). Perepletchikova *et al.* (2008) reviewed the evidence of family therapies specifically on alcohol use, though some of the family therapies did include substance use disorders. The types of family therapies included: multi systemic therapy, multidimensional therapy, brief family therapy, functional family therapy and strength oriented family therapy. The review reported that multi-component therapy again showed some benefits over standard group therapy for substance misuse and criminal activity outcomes.

6.26.7 Evidence summary

The evidence for the use of multi-component interventions demonstrates clear benefits on offending behaviour and promising results for the reduction of alcohol and drug misuse. As was found with the individual- or group-based interventions, much of the research focuses on children and young people with substance use disorders and who are more likely have comorbid psychiatric disorders. Although not specifically focused on alcohol this does not significantly detract from their applicability to this guideline as comorbidity with conduct

disorder and poly-drug use is a common feature amongst adolescents with significant alcohol misuse. The research to date however does not favour one particular multi-component intervention over another for the treatment for alcohol use disorders.

6.26.8 Review of pharmacological interventions for children and young people

The pharmacological review for adults identified that both acamprosate and naltrexone were clinically effective and cost effective in the treatment of moderate to severe alcohol dependence. The GDG were able to identify 3 small pilot RCTs in this area for children and young people (Niederhofer & Staffen, 2003a, Niederhofer *et al.,* 2003b, and Niederhofer & Staffen, 2003c). A narrative synthesis was conducted by the review team in order to assess the efficacy of pharmacological interventions for children and young people.

Niederhofer & Staffen (2003) conducted a double blind placebo controlled study with 26 participants with a DSM-IV diagnosis of chronic or episode alcohol dependence. Participants ranged in age from 16-19 years. The participants were randomly allocated to treatment with acamprosate (1332 mg daily) or placebo for 90 days. Participants were assessed at start of treatment, and at 30 and 90 days. Results revealed that the acamprosate group had a significantly higher proportions of days abstinent throughout the 90 days of treatment ($p<0.001$), as well as a higher duration of mean cumulative abstinence ($p<0.01$). There were no significant differences between the two groups with regards to side effects, and diarrhoea was the only reported side effect.

Niederhofer and colleagues (2003c) assessed naltrexone compared to a placebo in a double blind placebo controlled study, with 30 participants ranging in age from 15-19 with a DSM-IV diagnosis of chronic or episodic alcohol dependence. All participants received 50mg of naltrexone daily and were assessed at the start of treatment and at 30 and 90 days. At the 90 day assessment point, sixty of ninety participants completed treatment. Participants remained abstinent longer than those in the placebo group during 90 days of treatment ($p<0.01$) and had a longer duration of mean cumulative abstinence (69.8 days) than the placebo arm (22.8 days) ($p<0.01$). It must be noted that it is not clear from the paper how many participants were randomised to each group; therefore the findings should be interpreted with caution.

Lastly, Niederhofer & Staffen (2003c) compared disulfiram and placebo in a double blind placebo controlled trial with 26 adolescents (age range: 16-19) with DSM-IV chronic or episodic alcohol dependence. Participants received 200mg of disulfiram daily and were assessed at the start of treatment, 30 and 90 days. Twenty-six of the 49 participants recruited completed the 90 days of double-blind treatment. Results indicated that on day 90 of treatment, 20 of the placebo treated patients compared with 7 disulfiram treated patients had been continuously abstinent ($p=0.0063$). Additionally, the duration of mean cumulative abstinence was significantly higher in the disulfiram group (68.5 days) than in the placebo group (29.7 days) ($p=0.012$).

6.26.9 Evidence summary

Taken together, there is little evidence based on the results of three small RCTs to assess the efficacy of pharmacological interventions in young people and adolescents. The three small pilot studies do, however, provide some preliminary data indicating positive responses in young people and adolescents for pharmacological interventions when compared to placebo. Due to the poor methodological quality of these studies however, results should be interpreted with very considerable caution. As a result, any recommendations for young people and adolescents can only be extrapolated from the data set for adults.

6.26.10 Evidence into recommendations

This section draws together the evidence summaries for assessment and case identification, management of withdrawal and treatment interventions for children and young people with harmful alcohol misuse and dependence. The evidence base is limited and as a consequence the GDG were required to extrapolate from a number of data sets which did not directly address the treatment brief alcohol related problems in children and young people including data on adults with alcohol problems (for the withdrawal management) and substance misuse and conduct disorder for the treatment interventions. However, the GDG considered this to be justified approach as there is an urgent need to provide recommendations for the treatment of the increasing problem of adolescent alcohol misuse. In extrapolating from these data sets the GDG adopted a cautious approach, recognising that as new evidence emerges the recommendations in this guideline will need revision.

Assessment and case identification

The GDG decided to adopt a modified version of the assessment framework adopted for adults. As with the adult review the GDG favoured the use of the AUDIT tool as a case identification/screening device and this is consistent with the approach adopted the NICE prevention and brief intervention guideline (NICE, 2010a) However, thr GDG decide to adjust the threshold for the AUDIT tool in light of evidence that this increased the sensitivity for adolescent alcohol misuse. For a more comprehensive assessment the GDG recommended two possible assessment tools and the integration of any assessment of alcohol misuse into a comprehensive assessment of the needs of the child or young person.

Management of withdrawal

The primary concerns of the GDG here was with the identification of potential dependence and subsequent withdrawal. This leads to a lower threshold for possible detection of dependence and withdrawal as was the situation with case identification. Recommendations for treatment drew on the existing adult literature and as a consequence considerable caution is needed in the management of withdrawal which the GDG determined was best done in an inpatient setting.

Treatment interventions

Despite limited evidence a reasonably clear picture emerged about the effectiveness of interventions to promote abstinence and prevent replace in children and young people. There was some evidence for individual interventions such as CBT and less so for MET. There was stronger evidence for the use of multi-component interventions such as MST, FFT, SBSFT, and

MDFT but little evidence to determine whether one of other of the interventions had any advantage over the other. This evidence also mirrored the evidence for effectiveness in adults The GDG therefore decided that both types of intervention should be made available with CBT reserved for case where comorbidity is not present or of little significance but where it is present that multi-component interventions should be adopted.

In the absence of any convincing evidence on pharmacological interventions with adolescents the GDG decided to draw on the adult evidence base.

6.26.11 Recommendations

Assessment and interventions for children and young people who misuse alcohol

Assessment

6.26.11.1 If alcohol misuse is identified as a potential problem in children or young people aged 10 years and older, conduct an initial brief assessment to assess:

- the duration and severity of the alcohol misuse (the threshold on the AUDIT for referral and intervention should be lower for young people aged 10–16 on the basis of the more harmful effects of a given level of alcohol consumption in this population)
- any associated health and social problems
- the potential need for assisted withdrawal.

6.26.11.2 Refer all children and young people aged 10 years and older who misuse alcohol to a specialist child and adolescent mental health service (CAMHS) service for a comprehensive assessment of their needs.

6.26.11.3 A comprehensive assessment for children and young people (supported if possible by additional information from a parent or carer) should assess multiple areas of need, be structured around a clinical interview using a validated clinical tool (such as the ADI36 or the T-ASI37), and cover the following areas:

- consumption, dependence features, patterns of drinking

[36] Adolescent Diagnostic Interview: Winters, K. & Henly, G. (1993) *Adolescent Diagnostic Interview (ADI) Manual*. Los Angeles: Western Psychological Services.

[37] Teen Addiction Severity Index: Kaminer, Y., Burkstein, O.G. & Tarter, R.E. (1991) The Teen Addiction Severity Index: rationale and reliability. *International Journal of the Addictions, 26*, 219-226.

- comorbid substance misuse (consumption and dependence features) and associated problems
- mental and physical health problems
- peer relationships and social and family functioning
- developmental and cognitive needs, and educational attainment and attendance
- history of abuse and trauma
- risk to self and others
- readiness to change and belief in the ability to change
- obtaining consent to treatment
- formulation of a care plan and risk management plan.

Assisted withdrawal

6.26.11.4 Offer inpatient care to children and young people aged 10 years and older who need assisted withdrawal.

6.26.11.5 Base assisted withdrawal for children and young people aged 10 years and older on the recommendations for adults in this guideline (see section 5.27) and in NICE guideline 100. Adjust drug regimens to take account of age, height and body mass, and development of the child or young person.

Promoting abstinence and relapse prevention

6.26.11.6 For all children and young people aged 10 years and older who misuse alcohol, the goal of treatment should usually be abstinence in the first instance.

6.26.11.7 For children and young people aged 10 years and older who misuse alcohol offer:

- individual cognitive behavioural therapy for those with limited comorbidities and good social support
- multicomponent programmes (such as multidimensional family therapy, brief strategic family therapy, functional family therapy or multisystemic therapy) for those with significant comorbidities and/or limited social support. **[KPI]**

6.26.11.8 After a careful review of the risks and benefits, specialists may consider offering acamprosate or oral naltrexone in combination with cognitive behavioural therapy to young people aged between 16 and 18 years who have not engaged with or benefited from a multi-component treatment programme.

Delivering psychological and psychosocial interventions

6.26.11.9 Multidimensional family therapy should typically consist of 12–15 family-focused structured treatment sessions over 12 weeks. There should be a strong emphasis on case coordination and, if necessary, crisis management. As well as family sessions, individual interventions may be provided for both the child or young person and the parents. The intervention should aim to improve:

- alcohol and drug misuse
- the child or young person's educational and social behaviour
- parental well-being and parenting skills
- relationships with the wider social system.

6.26.11.10 Brief strategic family therapy should typically consist of fortnightly meetings over 3 months. It should focus on:

- engaging and supporting the family
- using the support of the wider social and educational system
- identifying maladaptive family interactions
- promoting new and more adaptive family interactions.

6.26.11.11 Functional family therapy should be conducted over 3 months by health or social care staff. It should focus on improving interactions within the family, including:

- engaging and motivating the family in treatment (enhancing perception that change is possible, positive reframing and establishing a positive alliance)
- problem solving and behaviour change through parent training and communication training
- promoting generalisation of change in specific behaviours to broader contexts, both within the family and the community (such as schools).

6.26.11.12 Multisystemic therapy should be provided over 3–6 months by a dedicated member of staff with a low caseload. It should:

- focus specifically on problem-solving approaches with the family
- use the resources of peer groups, schools and the wider community.

6.26.12 Research Recommendation

6.26.12.1 What methods are most effective for assessing and diagnosing the presence and severity of alcohol misuse in children and young people?

This question should be answered in a programme of research that uses a cross-sectional cohort design testing:

a) the sensitivity and specificity of a purpose designed suite of screening and case identification measures of alcohol misuse against a diagnostic gold standard (DSM-IV or ICD-10)

b) a purpose designed suite of measures to assess their reliability and validity in characterising the nature and the severity of the alcohol misuse in children and young people and which also determines their predictive validity in identifying the most effective treatment when compared with current best practice.

Particular attention should be paid to the feasibility of the measures in routine care and the training required to obtain satisfactory levels of accuracy and predictive validity. The programme needs to be large enough to encompass the age range (10 to 18 years) and the comorbidity that often accompanies alcohol misuse in children and young people.

Why this is important?

Alcohol misuse is an increasingly common problem in children and young people. However, diagnostic instruments are poorly developed or not available for children and young people. In adults there is a range of diagnostic and assessment tools (with reasonable sensitivity and specificity, and reliability and validity) that are recommended for routine use in the NHS to both assess the severity of the alcohol misuse and to guide treatment decisions. No similar well-developed measures exist for children and young people with the result that problems are missed and/or inappropriate treatment is offered. The results of this study will have important implications for the identification and the provision of effective treatment for children and young people with alcohol-related problems in the NHS.

7. Pharmacological interventions for treatment and management of alcohol misuse

7.1 Introduction

Pharmacological interventions can be involved in different stages of treating alcohol misuse and its consequences. Medication is recognised as an adjunct to psychosocial treatment to provide an optimum treatment package to improve physical and mental health (Casswell, 2009). Prescribed medications are not a stand-alone treatment option and are only recommended as part of care-planned treatment (MoCAM, DH, 2006; Woody, 2003; Berglund, 2005; Raistrick at al, 2006). This chapter aims to detail the utility and efficacy of pharmacological interventions in the treatment of alcohol misuse. The chapter focuses on the use of pharmacological interventions in the promotion of abstinence and the reduction in alcohol consumption, and the treatment of comorbid disorders. For the use of pharmacological interventions in a planned withdrawal programme see Chapter 5 and for the use of pharmacological interventions in an unplanned withdrawal programme see NICE guideline on management of alcohol-related physical complications (NICE, 2010).

7.1.1 Current practice

Pharmacotherapy is most frequently used to facilitate withdrawal from alcohol in dependent drinkers; many fewer individuals receive medication for relapse prevention such as acamprosate, disulfiram or naltrexone. Indeed some people may be reluctant to take medication and traditionally many residential rehabilitation units been not been prepared to accept or support people taking such medication, although this is slowly changing. A US survey revealed that only about 9% of people needing treatment for alcohol dependence received medication for relapse prevention; prescriptions of disulfiram declined by 3% between 2003 and 2007while prescriptions for naltrexone rose by 3% and for acamprosate by 10% (Mark et al, 2009). The level of prescribing is likely to be a similar or even lower in the UK. One estimate from data on prescriptions shows in 2008 that there were almost 135,000 prescriptions for acamprosate or disulfiram from primary care or NHS settings, with the majority (62%) for acamprosate (The NHS Information Centre, Lifestyles Statistics, 2009). In NHS hospitals, the use of disulfiram has increased and now slightly more (54%) prescriptions are issued than for acamprosate. There are regional variations with London issuing 104 prescriptions per 100,000 population and North East, 417. Some doctors can be reluctant to prescribe pharmacological interventions such as acamprosate, naltrexone and disulfiram, due to lack of knowledge or familiarity (Mark et al, 2003). Barriers to prescribing naltrexone in the US have been described as including a 'lack of awareness, a lack of evidence of efficacy in practice, side effects, time for patient management, a reluctance to take medications, medication addiction concerns, Alcoholics Anonymous (AA) philosophy, and price' (Mark et al, 2003). Nevertheless there are a

variety of medications with proven effectiveness and others with emerging efficacy that deserve due consideration as part of any individual treatment package.

For relapse prevention, both acamprosate and disulfiram are licensed for relapse prevention in the UK, much of Europe, Australasia and North America. Naltrexone is used in the UK but licensed elsewhere (for example, in the US).

In this guideline some pharmacotherapies described do not have a UK license for the indication discussed. It is important to realise that in this area of medicine, the absence of a license can mean that a license has not been applied for, rather than that the pharmacotherapy is not safe or appropriate. The terms 'unlicensed' and 'off-label' should not necessarily be taken to automatically imply disapproval, nor incorrect or improper use. There is no contra-indication to prescribing a drug off-license provided there is a body of evidence that supports its efficacy and safety (Healy and Nutt, 1998; Royal College of Psychiatrists report, 2007), and often evidence of safety may come from its use in other disorders where a license may have been granted. In particular, many drugs will not have a license for use in adolescents/children or in the elderly but this is does not mean they necessarily lack efficacy or are unsafe. Nevertheless, when prescribing in these populations due care must be taken in terms of dosage and monitoring of side effects, as well as potential interactions with other medications or physical morbidity (see section 1.6.1).

7.1.2 The effects of alcohol on brain chemistry and how this relates to medication.

As described in Chapter 2, alcohol affects many of the brain's chemical systems. The pharmacology of most of the medications commonly used such as benzodiazepines for alcohol withdrawal and disulfiram, acamprosate and naltrexone for relapse prevention, is well characterised and provides a potential neurobiological rationale for their effectiveness. Understanding more about how alcohol interacts with the brain has revealed many potential targets of interest, for example, to reduce drinking or craving. In many cases, medication already exists with the desired pharmacology but is used for another indication, for example, baclofen as an antispasmodic. Most new medication is being developed to prevent relapse rather than for use in alcohol withdrawal, or to improve cognition or prevent toxicity.

7.1.3 Brain chemistry and medication for relapse prevention

Dopamine

The pleasurable effects of alcohol are principally mediated by an increase in activity in the mesolimbic dopaminergic system. This dopaminergic system is regarded as the 'reward' pathway and is involved in 'natural' pleasures and motivations or drives such as food, sex and also responses to stress (Koob & Volkow, 2010).

As dependence develops to any substance, this dopaminergic system is involved in responding to significant or salient cues and motivation to take more (Schultz, 2007). Therefore, increases in dopaminergic activity arise when a 'cue' such as a pub or glass of favourite drink appears, which drives the person to seek alcohol. Some individuals may describe this as craving though for many they may not be consciously aware of it. Therefore the role of dopamine switches from signalling pleasure to 'alcohol-seeking or motivation' in response to a cue. In addition, activity

is reduced in the dopaminergic system in alcohol dependence and is associated with greater risk of relapse as well as symptoms of dysphoria (Heinz, 2002).

Since increases in dopamine mediate reward or motivation, blocking or antagonising the dopaminergic system, for example, with antipsychotics has been tried as a strategy to reduce drinking. However, these drugs have not shown clinical widespread effectiveness. Alternatively, since dependence is associated with reduced dopaminergic activity, boosting the dopamine system would be a reasonable strategy. Bromocriptine, a dopamine agonist, has shown promise in a clinical trial associated with a particular polymorphism of one of the dopamine receptors (Lawford et al, 1995) but not in all studies (Naranjo et al, 1997). It is possible for a drug to act like an agonist when there is low activity in the tissue and act like an antagonist when there is high activity – these are called partial agonists. One example is aripiprazole which is an antipsychotic. Preliminary studies have shown limited promise in relapse prevention (Anton et al, 2008; Martinotti et al, 2009).

Disulfiram may be one medication that has some effects through the dopaminergic system in the brain. The effect of disulfiram is to block an enzyme (aldehyde dehydrogenase) in the liver that is involved in metabolising or getting rid of alcohol. Blocking this enzyme causes an unpleasant reaction involving flushing, nausea, palpitations etc. However, the enzyme in the brain that turns dopamine into noradrenaline is from the same family as the liver enzyme and so is also blocked by disulfiram leading to an increase in dopamine (Gaval-Cruz & Weinshenker, 2009). Whether this increase is linked to disulfiram's effectiveness remains unproven.

Opioid system

Alcohol increases levels of endorphins or opiates in the brain, which in turn increase dopaminergic activity. The main opiate receptor involved in 'alcohol-liking' is mu, but the other opiate receptors, kappa and delta, also appear to have some role in alcohol liking and dependence (Herz, 1997).

Consequently opiate antagonists or blockers, such as naltrexone or nalmefene, have been used to try and treat alcohol problems. Naltrexone is a non-specific opiate antagonist, blocking mu, kappa and delta receptors, whilst nalmefene is a mu antagonist and possibly a kappa partial agonist (Bart et al, 2005). Both of these medications, though naltrexone is more widely used, can reduce the pleasurable effects of alcohol (Drobes et al, 2004). A polymorphism of the mu opioid receptor has been reported to be predictive of treatment response to naltrexone in some studies (Anton et al, 2008).

GABA – glutamate systems

The GABA system is the brain's inhibitory or calming chemical system. Stimulation of one of its receptors, the GABA-B, reduces dopaminergic activity in the so-called reward pathway and therefore drugs that boost this system have been shown to reduce drug-liking and seeking (Cousins et al, 2002). Baclofen is a medication that has long been used to treat muscle spasms and acts as a GABA-B agonist, for example it will boost activity. This mechanism is proposed to underlie baclofen's recently reported efficacy in relapse prevention for alcohol dependence (Addolorato et al, 2007).

The glutamatergic system is the brain's excitatory system and is involved in modulating the dopaminergic reward pathway. Acamprosate is a drug used for maintaining abstinence and has been shown to primarily reduce glutamatergic activity in the brain with some effect on increasing GABA-ergic activity. Since alcohol dependence is associated with hyperactivity in the glutamatergic system and reduced GABA-ergic activity, acamprosate may also improve abstinence rates by 'normalising' this imbalance (Littleton, 2000). It is also suggested that in abstinence, conditioned withdrawal (a withdrawal-like state such as anxiety induced by an object or place previously associated with drinking) is associated with a similar GABA-glutamatergic imbalance. Such conditioned withdrawal may be experienced as craving and acamprosate is proposed to also 'correct' this imbalance (Littleton, 2000). More recently roles in relapse prevention for other glutamatergic receptor subtypes for example, mGLuR2/3 and mGLuR5 have begun to be characterised (Olive, 2009). To reduce glutamatergic activity, memantine, a blocker or antagonist of one of glutamate's receptors, NMDA, has been investigated but not shown efficacy in preventing relapse (Evans et al, 2007).

Anticonvulsants such as topiramate, can also reduce glutamatergic activity and boost GABA activity. In addition they can alter ion (calcium, sodium, potassium) channel activity thus further reducing brain activity. Several anticonvulsants are being studied for efficacy in treating alcohol misuse with currently the most evidence for topiramate (Johnson et al, 2007). Of the newer anticonvulsants, gabapentin and its analogue pregabalin have received some attention since they appear to have some efficacy in treating a variety of disorders commonly seen in those with alcohol problems such as depression, anxiety or insomnia. Both medications are licensed for use in epilepsy, neuropathic pain, and pregabalin for generalised anxiety disorder. Despite their names, they have not been shown to have any effect on the GABA system. Although, there is some limited inconsistent evidence that pregabalin may interact with the GABA-B receptor (Landmark, 2007). Both gabapentin and pregabalin interact with the alpha2delta voltage-activated calcium channel subunits resulting in inhibition of excitatory neurotransmitter release, mostly glutamate (Landmark, 2007).

Hydroxybutyric acid (GHB) is a short-chain fatty acid which naturally occurs in the brain and GABA is its precursor. It has been used as an anaesthetic drug and to treat narcolepsy. Together with its pro-drug, butyrolactone (GBL), however, it is also a drug of abuse and is used as a club drug or by body-builders. The exact mechanisms of action in the brain are not clear, particularly around how it modulates reward pathways, but it has been suggested that it mimics alcohol.

Serotonergic system

The acute and chronic effects of alcohol on the serotonin system are complex and not fully understood. One consistent demonstration has been of reduced serotonergic activity in so-called 'early onset alcoholism' which describes individuals who become dependent before the age of 25 years old, have impulsive or antisocial personality traits, have a family history of alcoholism and are often male (Cloninger et al, 1981). In addition, many disorders which are commonly seen in individuals with alcohol problems are also proposed to have serotonergic dysfunction, for example, bulimia, depression, anxiety, OCD.

Since a dysfunctional serotonergic system is implicated in alcohol misuse, drugs that can modulate this system have been studied as treatments for preventing relapse. These include

serotonin specific reuptake inhibitor (SSRI) antidepressants and the anxiolytic, buspirone, a 5HT1A partial agonist. Such an approach is separate from any effect these drugs might have in treating any comorbid depression or anxiety for which they are licensed. Both SSRIs and buspirone have been found to reduce alcohol consumption in animal models (Johnson, 2008). However, for both SSRIs and buspirone, clinical efficacy in preventing relapse has been hard to demonstrate.

One particular serotonin receptor subtype, 5HT3, modulates the dopaminergic reward pathway. Blockers or antagonists of 5HT3 receptors reduce dopaminergic activity, which results in reduced alcohol drinking in animal models. Therefore, ondansetron, a 5HT3 antagonist used to treat nausea, has been studied and clinical efficacy has been shown for some doses, more so in early-onset alcoholism (Johnson et al, 2000). Critical roles for the other serotonin receptors in alcohol use and dependence have not been demonstrated.

7.1.4 Brain chemistry and medication for alcohol withdrawal.

A significant number of alcohol's effects on the brain involve interacting with the inhibitory GABA system. In addition to the GABA-B system described above, there is a GABA-A or GABA-benzodiazepine system that plays several important roles in mediating effects of alcohol on the brain.

The GABA-A receptor is made of different subunits on which there are various binding sites, for benzodiazepines, barbiturates, neurosteroids, some anaesthetics as well as for GABA. Alcohol interacts with the GABA-benzodiazepine receptor and increases its inhibitory activity, resulting in reduced anxiety and sedation, and can contribute to ataxia, slurred speech and respiratory depression. Thus alcohol has a similar effect to benzodiazepines such as diazepam. Alcohol is often used for its anxiolytic or sedative effects rather than pleasurable effects and anxiety and sleep disorders are associated with vulnerability to alcohol misuse.

Tolerance is the need to drink more alcohol to get the same or desired effect develops in those drinking more heavily and regularly. A reduced sensitivity of the GABA system to alcohol underlies tolerance. It is thought that changes in the subunit profile of the GABA-A receptor complex are involved (Krystal et al, 2006). In alcohol withdrawal, benzodiazepines such as chlordiazepoxide (Librium) or diazepam (Valium) will boost this reduced GABAergic function to increase the inhibitory activity in the brain. This is important to control symptoms such as anxiety, tremor and to reduce the risk of complications such as seizures, delirium tremens.

In addition to boosting the inhibitory GABA system, alcohol antagonises the excitatory neurotransmitter system, glutamate and particularly the NMDA receptor. To overcome this blockade, the number of NMDA receptors increase in response to continued drinking. This increase has been associated with memory impairment in animal models and may therefore underlie amnesia or blackouts, which can be experienced by people who drink heavily (Krystal et al, 2003). In alcohol withdrawal, therefore the increased glutamatergic activity significant contributes to the associated symptoms and risk such tremor and seizures. Anticonvulsants which reduce glutamatergic activity as well as increasing GABA-ergic activity, can therefore be used to treat alcohol withdrawal. In addition to this GABA-glutamate activity, anticonvulsants

will also inhibit voltage-activated sodium channels and, consequently, further excitatory activity.

Another consequence of increased glutamatergic and calcium channel activity is cell death. Therefore a potential advantage of antagonising this increased activity in withdrawal is neuroprotection or preventing cell death. In animal models, acamprosate has been shown to reduce increased glutamatergic activity in withdrawal but robust clinical evidence is lacking. Whether it occurs with anticonvulsants has not been systematically studied.

7.2 Review of pharmacological interventions

The focus of this section is on the use of pharmacological interventions to prevent relapse or reduce alcohol consumption. The GDG therefore focused the search on studies of interventions that supported these aims. The use of drugs alone or in combination with a range of other psychosocial interventions where considered. The drugs set out in Table 1 were considered in this review

Table 88. Pharmacology of medications for the treatment of alcohol misuse

Medication	Main target - system and action	Other relevant targets	Use in which stage
Acamprosate	Antagonises glutamatergic function (NMDA, mGLuR5)	Increases GABA-ergic function	Relapse prevention
Naltrexone	Opiate antagonist		Relapse prevention
Disulfiram	Blocks aldehyde dehydrogenase in liver increasing acetaldehyde	Blocks dopamine-B-hydroxylase in brain, increasing dopamine	Relapse prevention
Antipsychotics – variety of 'first or second generation'.	Dopamine DRD2 antagonists (eg olanzapine, quetiapine); partial agonist (eg aripiprazole)		Relapse prevention, antipsychotic
Benzodiazepines	Increases GABA-benzodiazepine function		Medically assisted withdrawal, possible role in relapse prevention.
Baclofen	GABA-B agonist		Relapse prevention,
Gabapentin	Ca channel antagonist		Relapse prevention and

			withdrawal
Pregabalin	Ca channel		Relapse prevention
Topiramate	Increases GABA-ergic function and antagonises some glutamate.	Reduces excitatory ion channel activity	Relapse prevention
Memantine	NMDA antagonist		Relapse prevention.
Odansetron	5HT3 antagonist		Relapse prevention
Antidepressants: SSRI eg sertraline	5HT reuptake inhibitor		Relapse prevention, antidepressant, anxiolytic
Buspirone	$5HT_{1A}$ partial agonist		Relapse prevention, anxiolytic

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2 ### 7.2.1 Databases searched and inclusion/exclusion criteria

3 Information about the databases searched and the inclusion/ exclusion criteria used for this
4 section of the guideline can be found in Appendix 16e (further information about the search for
5 health economic evidence can be found in Chapter 3).

Table 89. Databases searched and inclusion/exclusion criteria for pharmacological interventions

Primary clinical questions	For people with alcohol dependence or harmful alcohol what pharmacological interventions are more clinically and cost-effective? What are the impacts of severity and comorbities on outcomes? When should pharmacological treatments be initiated and for what duration should they be prescribed?
Electronic databases	MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Library
Date searched	Database inception to March 2010
Study design	RCTs
Patient population	At least 80% of the sample meet the criteria for alcohol dependence or harmful alcohol use (clinical diagnosis or drinking > 30 drinks per week)
Excluded populations	Hazardous drinkers and those drinking <30 drinks per week Pregnant women
Interventions	Any pharmacological treatment of alcohol use disorder
Comparator	Any other intervention
Critical Outcomes	Discontinuing treatment for any reason Discontinuing treatment due to adverse events Lapsing (returning to a drinking state) Relapsing (returning to a heavy drinking state) % days abstinent Cumulative abstinence duration Drinks per drinking day Total drinks consumed during treatment period Total days of heavy drinking during treatment Time to first drink Time to heavy drinking day

7.2.2 Studies considered[38]

The review team conducted a systematic search for RCTs that assessed the benefits and disadvantages of pharmacological interventions and related health economic evidence (see section 1.7).

The GDG decided to conduct a meta-analysis only on the drugs that were licensed for alcohol use in the UK or drugs that are in common usage with a large amount of clinical evidence on efficacy. From this criteria, the drugs identified for review were acamprosate, naltrexone and disulfiram. For naltrexone and disulfiram, only the oral delivery preparations of these drugs was considered for review due the lack of available evidence and the uncommon usage of the extended-release and subcutaneous implantation preparations of these drugs. For a narrative review on other pharmacological interventions for relapse prevention see Section 1.9.

[38] Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

A total of 136 references were identified by the electronic search relating to clinical evidence for acamprosate, naltrexone and disulfiram and a further 4 studies (all of acamprosate) were identified from other reviews. After further assessing these references on the basis of reading the full text, 53 of these references met the eligibility criteria set by the GDG. The remaining 87 studies were excluded from the analysis. Reasons for exclusion included not providing an acceptable diagnosis of alcohol dependence, not being an RCT, having less than 10 participants per group, not double blind and not reporting any relevant outcomes. Further information about both included and excluded studies can be found in Appendix 16e.

The GDG decided to exclude trials from the meta-analysis where the participant sample consisted of only young people under the age of 18, as this population was considered too different to compare to an adult population. These trials are reviewed in Chapter 6. In addition, trials where the participant sample included a very high prevalence of comorbid mental health disorders were excluded from the meta-analysis and are reviewed in section 1.10 as these trials were not typical of the trials included for analysis.

7.2.3 Acamprosate

There were a total of 19 trials (including 4 studies still awaiting translation) comparing acamprosate with placebo. These were typically large, high quality studies, of which 10 were sponsored by the drug company. A number of psychosocial interventions were used in addition to the trial medication, in line with the drug licensing agreement, which included alcohol counselling, medication management and relapse prevention as well as high intensity alcohol treatment programs. Data on participants lapsing to alcohol consumption was acquired from the authors of two meta-analyses (Mann et al, 2004; Rosner et al, 2008), who had access to unpublished data and therefore allowed for the development of a more complete data set. Both the PAILLE1995 and PELC1997 studies were three armed trials where two different doses of acamprosate were compared to placebo (1.3g and 2g). To avoid the double counting of the control data, we only used the data for the groups taking 2g of acamprosate, as this is the dose recommended by the BNF.

The population within these trials was typically presenting with moderate to severe dependence on alcohol, either indicated through alcohol consumption or dependency scale show at baseline. These studies were mainly conducted in Europe, with only one (CHICK2000) being conducted in the UK. Acamprosate was started after the participant completed medically assisted withdrawal (if required) in all trials except one, GUAL2001, when it was started during assisted withdrawal.

Study characteristics are summarised in Table 3, evidence from the important outcomes and overall quality of evidence are presented in Table 4. The full evidence profiles and associated forest plots can be found in Appendix 18d and Appendix 17d respectively.

Table 90. Summary of study characteristics for acamprosate versus placebo

	acamprosate vs. placebo	
Total no. of trials (total no. of participants)	19 RCTs (N = 4629)	
Study ID	ANTON2006 BALTIERI2003 BARRIAS1997 BESSON1998 CHICK2000A GEERLINGS1997 GUAL2001 KIEFER2003 LADEWIG1993 MORLEY2006 NAMKOONG2003	PAILLE1995 PELC1992 PELC1997 POLDRUGO1997 ROUSSAUX1996 SASS1996 TEMPESTA2000 WHITWORTH1996
Diagnosis	DSM or ICD diagnosis of alcohol dependence	
Baseline severity:	Units consumed per week Mean: 145.15 Range: 90 – 314.37	
Mean dosage	1998 mg per day.	
Length of treatment	Range: 8 weeks – 52 weeks	
Length of FU Only including papers reporting FU Measures)	Up to 12 months: ANTON2006 BESSON1998 GEERLINGS1997 PAILLE1995 POLDRUGO1997 SASS1996 WHITWORTH1996	Up to 18 months: PAILLE1995 Up to 24 months: WHITWORTH1996
Setting	Outpatient ANTON2006 BALTIERI2003 BESSON1998 CHICK2000 GEERLINGS1997 GUAL2001 MORLEY2006 NAMKOONG2003 PAILLE1995 PELC1997 POLDRUGO1997 SASS1996 TEMPESTA2000	Inpatient/Outpatient KIEFER2003 WHITWORTH1996

Treatment Goal (if mentioned)	Abstinence: GUAL2001 KIEFER2003 POLDRUGO1997

Table 91. Evidence summary table for trials of acamprosate versus placebo

	Acamprosate versus Placebo
Total number of studies (number of participants)	19 RCTs (N = 4629)
Study ID	ANTON2006 BALTIERI2003 BARRIAS1997 BESSON1998 CHICK2000A GEERLINGS1997 GUAL2001 KIEFER2003 LADEWIG1993 MORLEY2006 NAMKOONG2003 PAILLE1995 PELC1992 PELC1997 POLDRUGO1997 ROUSSAUX1996 SASS1996 TEMPESTA2000 WHITWORTH1996
Benefits	
Lapsed (participants returning to any drinking)	At 2 months: RR = 1.19 (0.76, 1.88) K=1, N=142 At 3 months: RR = 0.88 (0.75, 1.04) K=1, N=350 At 6 months: RR = 0.83 (0.77, 0.88) K=17, N=3964 At 12 months: RR = 0.88 (0.80, 0.96) K=4, N=1332

	At 18 months: RR = 0.94 (0.87, 1.02) K=1, N=350 At 24 months: RR = 0.92 (0.87, 0.98) K=1, N=448
Relapsed to heavy drinking	At 3 months: RR = 0.95 (0.86, 1.05) K=1, N=612 At 6 months: RR = 0.81 (0.72, 0.92) K=10, N=2654 At 12 months: RR = 0.96 (0.89, 1.04) K=1, N=612
% days abstinent	At 2 months: SMD = -0.10 (--0.43, 0.23) K=1, N=142 At 3 months: SMD = 0.00 (-0.16, 0.15) K=1, N=612 At 12 months: SMD = 0.00 (-0.20, 0.20) K=1, N=612
Cumulative abstinence duration	At 3 months: SMD = -2.75 (-7.51, 2.01) K=2, N=241 At 6 months: SMD = -0.29 (-0.41, -0.17) K=4, N=1134 At 9 months: SMD = -0.24 (-0.46, -0.03) K=1, N=330 At 12 months: SMD = -0.35 (-0.46, -0.24) K=4, N=1316 At 24 months:

	SMD = -0.34 (-0.66, -0.03) K=2, N=720
Time to first drink	SMD = -0.26 (-0.45, -0.06) K=3, N=738
Drinks per drinking day	SMD = -0.05 (-0.29, 0.20) K=2, N=258
% days without heavy drinking	SMD = -0.06 (-0.38, 0.27) K=1, N=142
Harms	
Discontinuation for any reason	RR = 0.90 (0.81, 0.99) K=15, N=4037
Discontinuation due to adverse events	RR = 1.36 (0.99, 1.88) K=12, N=3774

7.2.4 Evidence summary

There was a significant but small effect of acamprosate in promoting abstinence in participants when compared to placebo (RR = 0.83, 95% CI = 0.77 to 0.88). The effect was most pronounced at 6 months, but remained significant up to 12 months. In the one trial that continued up to two years (WHITWORTH1996) this small effect continued for up to 12 months after the termination of treatment. The number of individuals relapsing to heavy drinking was also significantly less in the acamprosate group. This effect was also small (RR = 0.90, 95% CI = 0.81 to 0.99) but suggests participants were more likely to stay in treatment if randomised to acamprosate instead of placebo. However, more participants left the trials due to adverse events in the acamprosate group, although this was not statistically significant.

The quality of the evidence for acamprosate is of high quality, therefore further research is unlikely to have an important impact on our confidence in the estimate of the effect.

7.2.5 Naltrexone

One study by Petrakis et al (2005) although a high quality trial, was excluded as the whole participant sample was comorbid with a range of axis I disorders, with many participants having multiple co-existing disorders. This was unusual when compared the included trials, where comorbidity was usually grounds for exclusion. This study is described more fully in the comorbidity in Section 1.10.

There were a total of 27 trials comparing oral naltrexone with placebo and 4 trials comparing naltrexone with acamprosate. In addition, there were two studies comparing naltrexone with naltrexone plus sertraline and one trial comparing naltrexone with topiramate. The majority of the trials were large, high quality studies with five trials sponsored by drug companies. 26 of the trials (LATT2002 being the exception) included one of a number of different psychosocial intervention in addition to either naltrexone or placebo, which included alcohol counselling, coping skills or relapse prevention as well as high intensity alcohol treatment programs.

Unpublished data on individuals relapsing to heavy drinking was acquired from the authors of a meta-analysis (Rosner et al, 2008), who had access to unpublished data.

The participant population included in these trials ranged from mild to severe dependence based on baseline alcohol consumption and dependency scale scores. This is in contrast to the studies included in the acamprosate review whether participants generally presented with more severe dependency. The majority of these trials were conducted in North America, and recruitment was most commonly through advertisements or referrals. If assisted withdrawal was required, then naltrexone was started after this was completed in these trials.

Study characteristics are summarised in Table 92, evidence from the important outcomes and overall quality of evidence are presented in Table 93. The full evidence profiles and associated forest plots can be found in Appendix 18d and Appendix 17d respectively.

Table 92. Summary of study characteristics for naltrexone

	Oral naltrexone vs. placebo	Oral naltrexone vs acamprosate	Oral naltrexone + sertraline vs oral naltrexone	Oral naltrexone vs topiramate
Total no. of trials (total no. of participants)	27 RCTs (N = 4296)	4 RCTs (N= 957)	2 RCTs (N=178)	1 RCT (N=101)
Study ID	AHMADI2002 ANTON1999 ANTON2005 ANTON2006 BALLDIN2003 BALTIERI2008 CHICK2000B GASTPAR2002 GUARDIA2002 HEINALA2001 HUANG2005 KIEFER2003 KILLEEN2004 KRANZLER2000 KRYSTAL2001 LATT2002 LEE2001 MONTI2001 MORLEY2006 MORRIS2001 OMALLEY1992 OMALLEY2003 OMALLEY2008 OSLIN1997 OSLIN2008 VOLPICELLI199	ANTON2006 KIEFER2003 MORLEY2006 RUBIO2001	FARREN2009 OMALLEY2008	BALTIERI2008

	2 VOLPICELLI1997			
Diagnosis	DSM or ICD diagnosis of alcohol dependence	DSM or ICD diagnosis of alcohol dependence	DSM or ICD diagnosis of alcohol dependence	DSM or ICD diagnosis of alcohol dependence
Baseline severity: mean Range	Units consumed per week Mean – 98.6 Range – 70.56 - 223	Units consumed per week Mean –128.1 Range: 74.3 - 223	Units consumed per week Mean –83.75 Range: 60 - 107.5	Units consumed per week Mean: 263.64
Mean dosage	naltrexone: 50mg daily	naltrexone: 50 mg daily acamprosate: 1998 mg per day	naltrexone: 50 mg daily Sertraline: 100mg per day	naltrexone: 50 mg daily topiramate: 300mg per day
Length of treatment	Range: 12 weeks – 24 weeks	Range: 12 weeks – 52 weeks	Range: 12 weeks – 16 weeks	12 weeks
Length of FU Only including papers reporting FU Measures)	Up to 6 months: ANTON1999 KIEFER2003 OMALLEY1999 Up to 12 months: ANTON2006	Up to 6 months: KIEFER2003 Up to 12 months: ANTON2006		

Setting	Outpatient AHMADI2002 ANTON1999 ANTON2005 ANTON2006 BALLDIN2003 BALTIERI2008 CHICK2000B GUARDIA2002 HEINALA2001 HUANG2005 KILLEEN2004 KRANZLER2000 KRYSTAL2001 LATT2002 MONTI2001 MORLEY2006 MORRIS2001 OMALLEY1992 OMALLEY2003 OMALLEY2008 OSLIN1997 OSLIN2008 VOLPICELLI1992 VOLPICELLI1997 Inpatient/Outpatient GASTPAR2002 KIEFER2003 LEE2001	Outpatient ANTON2006 MORLEY2006 RUBIO2001 Inpatient/Outpatient KIEFER2003	Outpatient FARREN2009 OMALLEY2008	Outpatient BALTIERI2008

Treatment Goal (if mentioned)	Abstinence ANTON2006 GUARDIA2002 HEINALA2001 (supportive therapy groups) KRANZLER2000 KRYSTAL2001 LEE2001 OMALLEY1992 OSLIN1997 Drinking Reduction/Moderation HEINALA2001 (Coping skills groups)	Abstinence ANTON2006 RUBIO2001	Not mentioned in any trials	Not mentioned in any trials

Table 93. Evidence summary table for trials of naltrexone

	Oral naltrexone vs placebo	Oral naltrexone vs acamprosate	Oral naltrexone + sertraline vs oral naltrexone	Oral naltrexone vs topiramate
Total number of studies (number of participants)	27 RCTs (N = 4164)	4 RCTs (N= 957)	2 RCTs (N=178)	1 RCT (N=101)
Study ID	AHMADI2002 ANTON1999 ANTON2005 ANTON2006 BALLDIN2003	ANTON2006 KIEFER2003 MORLEY2006 RUBIO2001	FARREN2009 OMALLEY2008	BALTIERI2008

	BALTIERI2008 CHICK2000B GASTPAR2002 GUARDIA2002 HEINALA2001 HUANG2005 KIEFER2003 KILLEEN2004 KRANZLER2000 KRYSTAL2001 LATT2002 LEE2001 MONTI2001 MORLEY2006 MORRIS2001 OMALLEY1992 OMALLEY2003 OMALLEY2008 OSLIN1997 OSLIN2008 VOLPICELLI1992 VOLPICELLI1997			
Benefits				
Lapsed (participants returning to any drinking)	At 3 months: RR = 0.92 (0.86, 1.00) K=17, N=1893 At 6 months (maintenance treatment): RR = 0.79 (0.60, 1.05) K=1, N=113	At 12 months: RR = 0.71 (0.57, 0.88) K=1, N=157	At 3 months: RR = 1.08 (0.77, 1.51) K=1, N=67	At 1 month: RR = 1.44 (0.88, 2.35) K=1, N=101 At 2 months: RR = 1.54 (1.02, 2.33) K=1, N=101 At 3

	At 6 months (follow up): RR = 0.90 (0.69, 1.17) K=1, N=84			months: RR = 1.48 (1.11, 1.97) K=1, N=101
Relapsed to heavy drinking	At 3 months: RR = 0.83 (0.76, 0.91) K=22, N=3320 At 6 months (endpoint): RR = 0.96 (0.79, 1.17) K=1, N=240 At 6 months (follow up): RR = 0.74 (0.60, 0.90) K=3, N=284 At 6 months (maintenance treatment): RR = 0.46 (0.24, 0.89) K=1, N=113	At 3 months: RR = 0.96 (0.87, 1.06) K=3, N=800 At 6 months: RR = 0.95 (0.64, 1.43) K=1, N=80 At 12 months: RR = 0.99 (0.91, 1.08) K=1, N=612	RR = 1.03 (0.73, 1.46) K=1, N=67	

	At 9 months (endpoint): RR = 0.74 (0.56, 0.98) K=1, N=116 At 12 months (follow up): RR = 0.95 (0.88, 1.03) K=1, N=618			
% days abstinent	At 3 months: SMD = -0.22 (-0.37, -0.07) K=9, N=1607 At 6 months: SMD = -0.25 (-0.51, 0.00) K=1, N=240 At 12 months: SMD = -0.11 (-0.42, 0.20) K=1, N=618	At 3 months: SMD = 0.04 (-0.21, 0.29) K=2, N=720 At 12 months: SMD = -0.11 (-0.27, 0.04) K=1, N=612	At 3 months: SMD = -0.12 (-0.79, 0.56) K=2, N=178	
Time to first drink	SMD = -0.07 (-0.21, 0.08) K=5, N=730	SMD = -0.09 (-0.34, 0.15) K=2, N=265		
Time to first heavy drinking episode	SMD = -0.32 (-0.68, 0.03) K=8, N=1513	SMD = -0.39 (-081, 0.03) K=2, N=265		SMD = 0.43 (0.04, 0.83) K=1, N=101
Cumulative abstinence duration	SMD = -0.12 (-0.39, 0.15)			SMD = 0.34 (-0.06, 0.73)

	K=2, N=217			K=1, N=101
Drinks per drinking day during study period	SMD = -0.28 (-0.44, -0.11) K=10, N=1639	SMD = -0.76 (-1.09, -0.44) K=1, N=157	SMD = -0.95 (-2.94, 1.04) K=2, N=178	
Heavy drinking episodes during study period	SMD = -0.43 (-0.82, -0.03) K=7, N=797		SMD = -0.23 (-0.71, 0.25) K=1, N=67	SMD = 0.33 (-0.064, 0.72) K=1, N=101
Total drinks consumed during study period	SMD = -0.32 (-0.70, 0.06) K=2, N=257			
Harms				
Discontinuation for any reason	RR =0.94 (0.84, 1.05) K=25, N=3926	RR =0.85 (0.72, 1.01) K=4, N=957	RR = 1.55 (1.00, 2.42) K=2, N=178	RR = 1.12 (0.68, 1.83) K=1, N=101
Discontinuation due to adverse events	RR = 1.79 (1.15, 2.77) K=12, N=1933	RR = 1.44 (0.63, 3.29) K=2, N=769	RR =2.92 (0.82, 10.44) K=2, N=178	

7.2.6 Evidence summary

The comparison of oral naltrexone versus placebo showed a small but significant effect favouring naltrexone on rates of relapse to heavy drinking (RR = 0.83, 95% CI = 0.75 to 0.91). The mean drinks per drinking day within the trial duration was less in the naltrexone group when compared to placebo with a small but significant effect (SMD = -0.28, 95% CI = -0.44 to -0.11). A significant but small effect favouring naltrexone was also found on days of heavy drinking during the trial (SMD = -0.43, 95% CI = -0.82 to -0.03). Although overall discontinuation rates favoured naltrexone over placebo, there was no significant difference between the two groups. However, participants were significantly more likely to leave treatment due to adverse events in the naltrexone group, with significantly fewer adverse events reported in the placebo group.

When comparing oral naltrexone and acamprosate, the four trials reviewed showed no significant difference in discontinuation for any reason or due to adverse event between the two interventions. On critical outcomes, there were no significant differences between naltrexone and acamprosate except for number of individuals returning to any drinking (RR = 0.71, 95% CI = 0.57 to 0.88) and drinks per drinking days (SMD = -0.76, 95% CI = -1.09 to -0.44). However, these findings were based only on one study (RUBIO2001) which found participants in the naltrexone group were significantly less likely to return to any drinking and consumed significantly less drinks per drinking day during the trial period. When comparing naltrexone with topiramate, the analysis showed no significant differences between the groups on any outcomes except number of participants continuously abstinent and weeks until first relapse, both outcomes favouring naltrexone. The analysis of naltrexone versus naltrexone plus sertraline showed no significant differences between the groups on any outcomes. However, discontinuation rates were less in the combination group.

The quality of the evidence reviewed for oral naltrexone versus placebo was of high quality, therefore further research is unlikely to an important impact on our confidence in the estimate of the effect. The quality of the evidence for naltrexone versus acamprosate was also high. However, the quality for the evidence for the naltrexone plus sertraline combination intervention versus naltrexone alone and for naltrexone versus topiramate is moderate, therefore further research is likely to have an important impact on our confidence in the estimate of these effects.

7.2.7 Acamprosate + Naltrexone (combined intervention)

Study characteristics are summarised in Table 7, evidence from the important outcomes and overall quality of evidence are presented in Table 8. The full evidence profiles and associated forest plots can be found in Appendix 18d and Appendix 17d respectively.

There were two trials comparing the combination of acamprosate and naltrexone with placebo, acamprosate alone and naltrexone alone. Both were large, multiple armed trials designed specifically to test the effects of the drugs in isolation and together. The KIEFER2003 trial included a population of severely dependent drinkers recruited from inpatient facilities; their mean preadmission consumption of alcohol was 223 units per week. The ANTON2006 study included a less severe population of dependent drinkers who were recruited through advertisements or clinical referrals; their mean preadmission consumption of alcohol was 97 units per week.

Table 94. Summary of study characteristics for naltrexone + acamprosate

	naltrexone + acamprosate vs. Placebo	naltrexone + acamprosate vs. Acamprosate	naltrexone + acamprosate vs. naltrexone
Total no. of trials (total no. of participants)	2 RCTs (N = 694)	2 RCTs (N= 688)	2 RCTs (N=694)
Study ID	ANTON2006 KIEFER2003	ANTON2006 KIEFER2003	ANTON2006 KIEFER2003
Diagnosis	DSM or ICD diagnosis of alcohol dependence	DSM or ICD diagnosis of alcohol dependence	DSM or ICD diagnosis of alcohol dependence
Baseline severity: mean (SD)	Units consumed per week Mean –160.05 Range: 97.1 – 223	Units consumed per week Mean –160.05 Range: 97.1 - 223	Units consumed per week Mean –160.05 Range: 97.1 - 223
Mean dosage	KIEFER2003: acamprosate = 1998 mg per day. naltrexone = 50mg per day ANTON2006: acamprosate = 3g per day. naltrexone = 100mg per day	KIEFER2003: acamprosate = 1998 mg per day. naltrexone = 50mg per day ANTON2006: acamprosate = 3g per day. naltrexone = 100mg per day	KIEFER2003: acamprosate = 1998 mg per day. naltrexone = 50mg per day ANTON2006: acamprosate = 3g per day. naltrexone = 100mg per day
Length of treatment	12 weeks	12 weeks	12 weeks
Length of FU Only including papers reporting FU Measures)	Up to 6 months: KIEFER2003 Up to 12 months: ANTON2006	Up to 6 months: KIEFER2003 Up to 12 months: ANTON2006	Up to 6 months: KIEFER2003 Up to 12 months: ANTON2006
Setting	Outpatient ANTON2006 Inpatient/Outpatient KIEFER2003	Outpatient ANTON2006 Inpatient/Outpatient KIEFER2003	Outpatient ANTON2006 Inpatient/Outpatient KIEFER2003
Treatment Goal (if mentioned)	Abstinence ANTON2006	Abstinence ANTON2006	Abstinence ANTON2006

Table 95. Evidence summary table for trials of acamprosate + naltrexone

	acamprosate + naltrexone vs Placebo	acamprosate + naltrexone vs acamprosate	acamprosate + naltrexone vs naltrexone

Total number of studies (number of participants)	2 RCTs (N = 694)	2 RCTs (N= 688)	2 RCTs (N = 694)
Study ID	ANTON2006 KIEFER2003	ANTON2006 KIEFER2003	ANTON2006 KIEFER2003
Benefits			
Relapsed to heavy drinking	At 3 months: RR = 0.78 (0.56, 1.09) K=2, N=694 At 6 months: RR = 0.44 (0.28, 0.69) K=1, N=80 At 12 months: RR = 0.97 (0.90, 1.05) K=1, N=614	At 3 months: RR = 0.93 (0.74, 1.17) K=2, N=688 At 6 months: RR = 0.64 (0.38, 1.06) K=1, N=80 At 12 months: RR = 1.02 (0.94, 1.10) K=1, N=608	At 3 months: RR = 1.03 (0.90, 1.17) K=2, N=694 At 6 months: RR = 0.67 (0.40, 1.12) K=2, N=80 At 12 months: RR = 1.02 (0.94, 1.10) K=1, N=612
% days abstinent	At 3 months: SMD = -0.09 (-0.42, 0.25) K=1, N=614 At 12 months: SMD = -0.09 (-0.25, 0.06) K=1, N=614	At 3 months: SMD = -0.08 (-0.29, 0.13) K=1, N=608 At 12 months: SMD = -0.11 (-0.27, 0.05) K=1, N=608	At 3 months: SMD = -0.04 (-0.20, 0.12) K=1, N=614 At 12 months: SMD = 0.02 (-0.18, 0.21) K=1, N=614
Harms			
Discontinuation for any reason	RR =1.00 (0.53, 1.90) K=2, N=694	RR = 0.92 (0.65, 1.32) K=2, N=687	RR = 1.09 (0.87, 1.37) K=2, N=694
Discontinuation due to adverse events	RR = 3.16 (1.03, 9.76) K=1, N=614	RR = 1.39 (0.34, 5.71) K=1, N=608	RR = 1.10 (0.50, 2.40) K=1, N=614

7.2.8 Evidence summary

There was no significant difference between the combination of acamprosate and naltrexone than either drug alone at reducing the likelihood of returning to heavy drinking at three

months (combination versus acamprosate: RR = 0.93, 95% CI = 0.74 to 1.17 ; combination versus naltrexone: RR = 1.03 (0.90 to 1.17) and the one trial continuing up to 12 months showed a preserved effect. In addition, there were no significant differences on any other outcomes between the combination group and either drug. The combined drug group were also equivalent to the placebo group on discontinuation rates and percentage days abstinent. Relapse rates at 6 months were significantly different with a moderate effect in favour of the combined intervention group (RR = 0.44, 95% CI = 0.28 to 0.69), however there was no difference between the groups in relapse rates at 3 months or 12 months.

The quality of the evidence is high; therefore further research is unlikely to an important impact on our confidence in the estimate of the effect.

7.2.9 Oral Disulfiram

Unlike the reviews of acamprosate and naltrexone, there was much less high quality evidence available on the efficacy and effectiveness of disulfiram, and for this reason the GDG decided to use open label trials in the meta-analysis of disulfiram.

The reason for this was that due to the disulfiram-ethanol reaction, a number of the studies had to be open-label for ethical reasons so that participants were aware that they were taking a substance that can cause potentially dangerous side effects when taken with alcohol. This also contributes to the psychological effect of disulfiram, where the fear of the chemical reaction is believed to be as important as the pharmacological effects of the drug in determining the efficacy of the intervention. The FULLER1979 and FULLER1986 trials adapted their trials for this purpose and randomised participants to either the full dose of disulfiram (250mg per day) or to 1mg of disulfiram with a placebo agent which has been judged to have no clinical effect.

Due to the age of some of the trials, inclusion criteria for diagnosis was also relaxed to include papers that did not explicitly mention the diagnosis tool used to determine eligibility to the trial. The Petrakis et al (2005) trial was also excluded from the meta-analysis as many participants had a range of axis I disorders.

Study characteristics are summarised in Table 9, evidence from the important outcomes and overall quality of evidence are presented in Table 10. The full evidence profiles and associated forest plots can be found in Appendix 18d and Appendix 17d, respectively.

There were a total of three trials comparing oral disulfiram to placebo (FULLER1979; FULLER1986; CHICK1992), one trial comparing oral disulfiram to acamprosate (LAAKSOEN2008), two trials comparing to naltrexone (DESOUSA2004; LAAKSONEN2008) and one trial comparing oral disulfiram to topiramate (DESOUSA2008). In addition, there was also one trial comparing disulfiram with counselling to counselling alone with no pharmacological intervention (GERREIN1973).

The severity of the participants included in these trials was not reported for the older trials, however in the more recent studies, dependency indicated through baseline consumption and dependency scales suggested that these participants were of moderate to severe dependency. The trials varied in country conducted in, with CHICK1992 being the only trial conducted in the UK. Three studies were conducted in America (FULLER1979;

FULLER1986; GERREIN1973), two were conducted in India (DESOUSA2004 ; DESOUSA2008) and the last in Finland (LAAKSONEN2008).

Table 96. Summary of study characteristics for oral disulfiram

	Oral disulfiram vs. placebo	Oral disulfiram vs acamprosate	Oral disulfiram vs naltrexone	Oral disulfiram vs topiramate	Oral disulfiram + counselling vs counselling
Total no. of trials (total no. of participants)	3 RCTs (N =859)	1 RCT (N=243)	2 RCTs (N=343)	1 RCT (N=100)	1 RCT (N=26)
Study ID	CHICK1992 FULLER1979 FULLER1986	LAAKSONEN2008	DESOUSA2004 LAAKSONEN2008	DESOUSA2008	GERREIN1973
Diagnosis	National Council on alcoholism diagnostic criteria or by an undefined diagnosis tool.	ICD diagnosis of alcohol dependence	DSM or ICD diagnosis of alcohol dependence	DSM diagnosis of alcohol dependence	Undefined diagnosis tool
Baseline severity: mean (SD)	Units consumed per week Mean –198.5 Range: 190 - 207	Units consumed per week Mean – 136.25	Units consumed per week Mean –111.35 Range: 86.45 – 136.25	Units consumed per week Mean –70	No details
Mean dosage	disulfiram = 250mg daily	disulfiram = 150 mg daily acamprosate = 1998mg daily	disulfiram= 200 mg daily naltrexone = 50mg daily	disulfiram = 250mg daily topiramate = 150mg daily	disulfiram = 250mg daily
Length of treatment	Range: 24 weeks – 52 weeks.	52 weeks	52 weeks	36 weeks	8 weeks
Length of FU Only including papers reporting FU Measures)	No follow-up data recorded	No follow-up data recorded	No follow-up data recorded	No follow-up data recorded	No follow-up data recorded
Setting	Outpatient CHICK1992 FULLER1979 Inpatient/Outpatient FULLER1986	Outpatient LAAKSONEN2008	Outpatient DESOUSA2004 LAAKSONEN2008	Inpatient/Outpatient DESOUSA2008	Outpatient GERREIN1973
Treatment Goal (if mentioned)	Abstinence FULLER1986	Abstinence LAAKSONENE2008	Abstinence DESOUSA2004 LAAKSONE	Abstinence DESOUSA2008	Not mentioned

1
2 **Table 97. Evidence summary table for trials of oral disulfiram**

	Oral disulfiram vs placebo/ 1mg disulfiram	Oral disulfiram vs acamprosate	Oral disulfiram vs naltrexone	Oral disulfiram vs topiramate	Oral disulfiram + counselling vs counselling
Total number of studies (number of participants)	3 RCTs (N =859)	1 RCT (N=243)	2 RCTs (N=343)	1 RCT (N=100)	1 RCT (N=26)
Study ID	CHICK1992 FULLER1979 FULLER1986	LAAKSONEN2008	DESOUSA2004 LAAKSONEN2008	DESOUSA2008	GERREIN1973
Benefits					
Lapsed (participants returning to any drinking)	At 12 months: RR = 1.05 (0.96, 1.15) K=2, N=492		At 12 months: RR = 0.18 (0.08, 0.42) K=1, N=100		At 2 months: RR = 0.86 (0.55, 1.34) K = 1, N=49
Relapsed to heavy drinking			At 12 months: RR = 0.28 (0.13, 0.59) K=1, N=100	At 12 months: RR = 0.23 (0.09, 0.55) K=1, N=100	
Abstinent days (per week or total days)	Total days change score: SMD = -0.45 (-0.86, -0.04) K=1, N=93	Abstinent days per week up to week 12: SMD = -1.11 (-1.52, -0.70) K=1, N=106 Abstinent days per week from week 12 to 52: SMD = -0.74 (-1.17, -0.31) K=1, N=91	Total days: SMD = -0.41 (-0.81, -0.02) K=1, N=100 Abstinent days per week up to week 12: SMD = -1.09 (-1.50, -0.68) K=1, N=107 Abstinent days per week from week 12 to 52: SMD = -0.74 (-1.17, -0.31)	Total days: SMD = -0.30 (-0.70, 0.09) K=1, N=100	

			K=1, N=91		
Time to first drink		SMD = -0.84 (-1.28, -0.40) K=1, N=89	SMD = -1.22 (-2.47, 0.02) K=2, N=189	SMD = -3.16 (-3.75, -2.56) K=1, N=100	
Time to first heavy drinking episode		SMD = -1.17 (-1.66, -0.68) K=1, N=77	SMD = -1.50 (-2.49, -0.51) K=2, N=180	SMD = -2.74 (-3.29, -2.19) K=1, N=100	
Drinks per drinking day during study period			SMD = -0.11 (-0.50, 0.28) K=1, N=100		
Alcohol consumed during study period	Units consumed in last 4 weeks of trial – change score: SMD = -0.16 (-0.58, 0.25) K=1, N=90 Units consumed per week in last 6 months of trial – change score: SMD = -0.35 (-0.75, 0.05) K=1, N=97 Total units consumed in last 6 months of trial – change score: SMD = -0.49 (-0.91, -0.07) K=1, N=118	Grams per week up to week 12: SMD = -1.06 (-1.44, -0.67) K=1, N=118 Grams per week from week 12 to 52: SMD = -0.66 (-1.12, -0.20) K=1, N=76	Grams per week up to week 12: SMD = -0.93 (-1.31, -0.56) K=1, N=124 Grams per week from week 12 to 52: SMD = -0.74 (-1.20, -0.28) K=1, N=78		
Harms					
Discontinuation for any reason	RR =1.15 (0.43, 3.12) K=1, N=406	RR =1.24 (0.71, 2.16) K=1, N=162	RR =1.27 (0.73, 2.19) K=2, N=262	RR =1.00 (0.26, 3.78) K=1, N=100	RR =0.46 (0.08, 2.56) K=1, N=49
Discontinuation due to			RR =3.00 (0.13,	RR =0.20	

adverse events			71.92) K=1, N=100	(0.01, 4.06) K=1, N=100	

7.2.10 Evidence summary

Oral disulfiram was not significantly different from placebo in preventing participants lapsing to alcohol consumption (RR = 1.05, 95% CI = 0.96 to 1.15). There was also no difference in rates of discontinuation between the two groups. However, LAAKSONEN2008 showed that, in comparison to acamprosate, disulfiram was significantly more likely to increase the time until participants first drank any alcohol (SMD = -0.84, 95% CI = -1.28 to -0.40) and drank heavily (SMD = -1.17, 95% CI = -1.66 to -0.68) and also decreased the amount of alcohol consumed and the number of drinking days. In comparison to naltrexone, disulfiram was also significantly more likely to increase the time to first heavy drinking day and the number of abstinent days. Participants in the naltrexone group were significantly more likely to return to any drinking (RR = 0.18, 95% CI = 0.08 to 0.42) or relapse to heavy drinking (RR = 0.28, 95% CI = 0.13 to 0.59) when compared to the oral disulfiram group, although this was based on two open label studies (DESOUSA2004; LAAKSONEN2008).

The comparison of disulfiram and topiramate also showed a significant difference in the number of participants relapsing to heavy drinking (RR = 0.23, 95% CI = 0.09 to 0.55), time to first drink and time to first relapse in favour of disulfiram, but this was based on just one open label study (DESOUSA2008). It may be that the psychological effects of knowing they were taking disulfiram may have contributed significantly to the results. The comparison of disulfiram with counselling versus counselling alone showed no significant differences between the groups on numbers of participants returning to drinking (RR = 0.86, 95% CI = 0.55 to 1.34).

The quality of the evidence was moderate; therefore further research is likely to have an important impact on our confidence in the estimate of the effect. The main reason for the lower quality of the evidence was that the studies reviewed were generally not conducted in a double blind trial.

7.3 Meta-regression on baseline alcohol consumption and effectiveness

Whilst effectiveness has been established for acamprosate and naltrexone, and to some extent for disulfiram, not everyone benefits from these medications. In order to give medication to those most likely to benefit as well as reducing inappropriate prescribing, studies have been examined for predictors of outcome. No trials have been explicitly set up to define predictors, rather post-hoc analyses have been performed looking for relationships between outcome and clinical variables.

Concerning acamprosate and naltrexone, it has been suggested that severity of dependence may influence outcome based on the type of patients in US (recruited by advert, do not generally require medication for assisted withdrawal) compared with European (recruited from treatment services, require medication for withdrawal) trials (Garbutt, 2009).

A number of researchers have reported on the potential relationship between severity of alcohol dependence at baseline and effectiveness of both acamprosate and naltrexone (Monterosso, 2001; Richardson et al, 2008). The GDG decided to investigate whether baseline severity was associated with the effectiveness of either of these drugs. Craving has often been used as a measure of severity, but within the trials included the meta-analyses, the amount of alcohol consumed was much more frequently reported in the baseline demographics and therefore baseline severity was used in the analysis measured as the number of alcohol units consumed per week by the study sample. An alcohol unit was defined as 8g or 10ml of alcohol, as per UK classification. In studies published outside of the UK, the number of baseline 'drinks' was converted into UK alcohol units.

A random-effects meta-regression was performed in Stata Version 9.2 (StataCorp, 2007) using the revised meta-regression command with restricted maximum likelihood estimation and the improved variance estimator of Knapp and Hartung (2003). Covariates that were examined included: baseline severity (measured as the mean baseline consumption of alcohol in units per week); the setting of the trial (inpatient or outpatient); the year the study was published; the recruitment strategy of the trial and the trial was conducted in North America or the rest of the world. The regression coefficients are the estimated increase in the effect size (log RR) per unit increase in the covariate(s). Negative effect sizes indicate that the intervention had a better outcome than the control group. A random effects model (DerSimonian & Laird, 1986) was used in the analyses to incorporate the assumption that the different studies are estimating different, yet related, treatment effects, and to incorporate heterogeneity beyond that explained by the covariate(s) included in the model.

Figure 1 shows the association between baseline alcohol consumption and effectiveness for the 20 trials of naltrexone versus placebo that included extractable information on baseline drinking. There is a statistically significant association between baseline alcohol consumption and effectiveness (regression coefficient -.004, 95% CI -.007 to -.0002), with 54.43% of the between-study variance explained by baseline severity (p = .04) (see table 11). To control for variables that may act as confounders, the following variables were entered into a multivariate model: setting, recruitment, country, and year. The results suggest that baseline severity remains a significant covariate (regression coefficient-.004, 95% CI-.007 to -.001), with 97.61% of the between-study variance explained (see table 12).

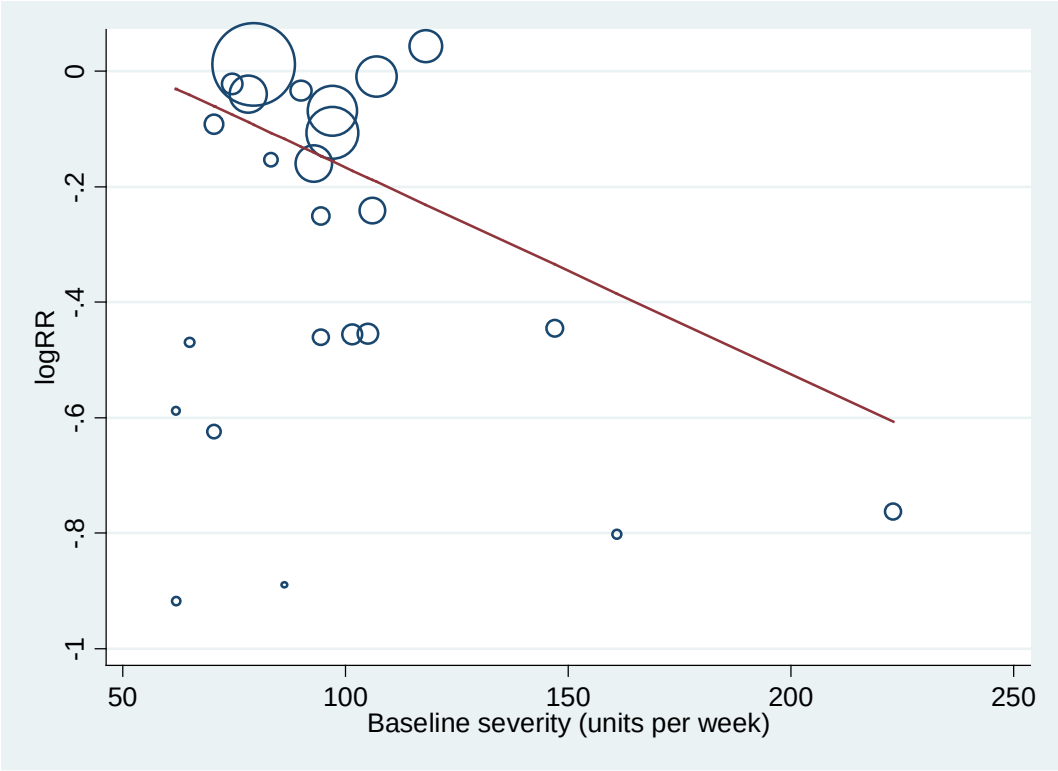


Figure 7. Association between baseline severity and effect size in naltrexone versus placebo trials (logRR)

Table 98. Results of univariate meta-regression in naltrexone versus placebo trials.

Variables	*k* (*n*)	Coefficient (Standard error)	95% CI	Adjusted *P*[a]
Baseline drinking	20 (3338)	-.003 (.002)	-0.007 to 0.001	.04
Constant		-.19 (.16)	-.15 to .53	.25

Abbreviations: CI, confidence interval; *k*, number of studies; *n*, number of participants.
[a]Calculated using the Higgins and Thompson Monte Carlo permutation test (10000 permutations).

Table 99. *Results of multiple covariate meta-regression in naltrexone versus placebo trials.*

Variables	*k* (*n*)	Coefficient (Standard	95% CI	Adjusted *P*[a]

		error)		
Baseline drinking	20		-0.007 to -	
	(3338)	-.004 (.002)	0.001	.02
Setting (inpatient/outpatient)	20			
	(3338)	-.16 (.17)	-0.51 to 0.19	.35
Recruitment strategy	20			
	(3338)	.05 (.13)	-0.22 to 0.31	.73
Country trial conducted	20			
	(3338)	.11 (.12)	-0.14 to 0.37	.37
Year published	20		-0.001 to	
	(3338)	.021 (.011)	0.043	.07
Constant		-41.64		
		(21.51)	-86.82 to 3.55	.07

Abbreviations: CI, confidence interval; *k*, number of studies; *n*, number of participants.
[a]Calculated using the Higgins and Thompson Monte Carlo permutation test (10000 permutations).

Figure 2 shows the association between baseline alcohol consumption and effectiveness in the 11 trials of acamprosate versus placebo that included extractable information on baseline drinking. The results suggest that there is no important association between baseline severity and effectiveness (regression coefficient -.0001, 95% CI -.0017 to .0015), with 0% of the between-study variance explained by baseline severity (p = .90) (see table 13). Baseline drinking was also found to have no association when controlling for the setting of the trial or the year the study was published (see table 14). Recruitment strategy and the country where the trial was conducted could not be tested as covarites as there was not enough variation on these areas in the studies to use these as covariates.

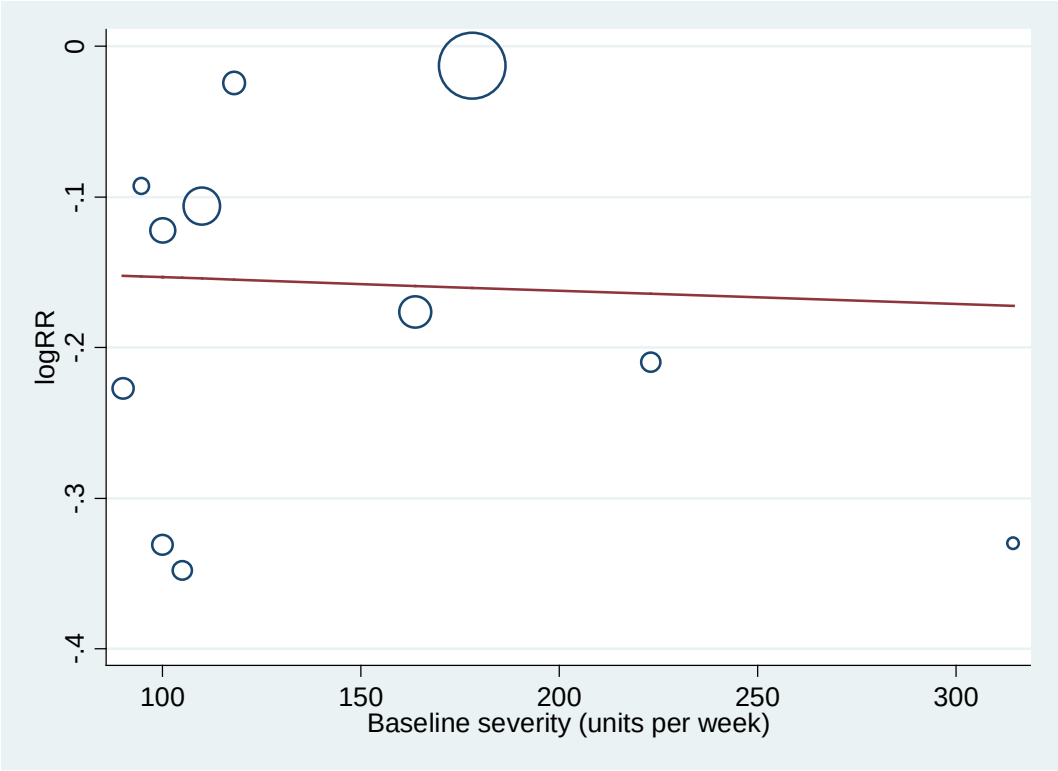


Figure 8. Association between baseline severity and effect size in acamprosate versus placebo trials (logRR)

Table 100. Results of univariate meta-regression in acamprosate versus placebo trials.

Variables	*k* (*n*)	Coefficient (Standard error)	95% CI	Adjusted *P*[a]
Baseline drinking	11 (3476)	- .0001(.0007)	-0.002 to -0.001	.9
Constant		-.14 (.11)	-.38 to .09	.2

Abbreviations: CI, confidence interval; *k*, number of studies; *n*, number of participants.
[a]Calculated using the Higgins and Thompson Monte Carlo permutation test (10000 permutations).

Table 101. Results of multiple covariate meta-regression in acamprosate versus placebo trials.

Variables	*k* (*n*)	Coefficient (Standard	95% CI	Adjusted *P*[a]

		error)		
Baseline drinking	11 (3476)	-.002 (.0008)	-0.002 to -0.001	.82
Setting (inpatient/outpatient)	11 (3476)	-.03 (.09)	-0.18 to 0.25	.72
Year published	11 (3476)	.01 (.013)	-0.02 to 0.04	.47
Constant		-19.3 (25.32)	-79.18 to 40.58	.47

Abbreviations: CI, confidence interval; *k*, number of studies; *n*, number of participants.
[a]Calculated using the Higgins and Thompson Monte Carlo permutation test (10000 permutations).

7.4 Predictors of efficacy

Acamprosate

Lesch and Walter (1996) reviewed outcomes in their trial with reference to their four typologies: Type I (social drinking develops into dependence, craving, relief drinking, family history); Type II (alcohol consumed to medicate sleep or anxiety; consumption varies with context, behaviour changes with alcohol); Type III (alcohol used to self-medicate a psychiatric disorder such as depression; family history positive for alcoholism or psychiatric disorder; impaired behaviours not always related to alcohol); and Type IV (brain damage and psychiatric disorders before 14yrs; seizures not related to alcohol; mild withdrawal symptoms). They reported that Types I and II, but not III and IV, responded to acamprosate.

In the UK trial, Chick (2000) speculated whether the continuous rather than episodic drinker would be more likely to respond since their negative study had more participants with episodic drinking patterns. Kiefer et al (2005) examined predictors in their original trial of acamprosate alone and with naltrexone and reported that acamprosate was mainly efficacious in patients with low baseline somatic distress, mainly effective in Type I, and that craving showed no predictive value.

Mason and Lehert (2010) explored the first US acamprosate trial (Mason et al, 2010) and suggested that acamprosate may reduce the negative impact of subsyndromal anxiety or a past psychiatric history.

In contrast, Verheul et al (2005) examined pooled data from seven RCTs that included 1485 patients with alcohol dependence. Whilst 'cumulative abstinence duration (CAD)', or

continuous abstinence, was predicted by higher levels of craving or anxiety at baseline, this was for all patients and acamprosate showed no differentially efficacy. Other variables that were investigated and showed no significant relationship with outcomes including severity of dependence which was non-linearly associated with CAD, family history, age of onset and gender. Therefore, they concluded that acamprosate is potentially effective for anyone with alcohol dependence.

Naltrexone

Monterosso et al, (2001) reported that those with a family history of alcoholism and high levels of craving were more likely to benefit from naltrexone. Rubio et al, (2005) similarly reported from their naltrexone trial that those with a family history of alcoholism benefited more, as well as those whose onset of alcohol abuse was before age 25, or those who had history of other substance abuse. Kiefer et al, (2005) reported that naltrexone was effective especially in patients with high baseline depression and in Type III and IV (Lesch & Walter, 2006).

Several studies have investigated whether genetic variants of the opioid receptors, mu, kappa and delta, are related to naltrexone's efficacy. Several studies have reported an association between greater treatment response and A118G (OPRM1), a functional polymorphism of the μ-opioid receptor gene, (Oslin et al 2003; Anton et al 2008; Oroszi et al 2009; Kim et al 2009) but not all (Gelenter et al, 2007). In a relatively small sample, Ooteman et al, (2009) explored other genotypes and reported effects of GABRA6, GABRA2, OPRM1 and dopamine D2 receptor genes moderated treatment response from acamprosate or naltrexone and subjective and physiological cue reactivity.

It is not clear whether gender influences treatment outcome with studies of naltrexone in alcoholism reporting no gender differences (Anton et al, 2006). Pettinati et al, (2008) reported that in comorbid cocaine/alcohol dependence naltrexone (150mg/d), men reduced their cocaine and alcohol use whereas women did not, indeed their cocaine use increased. However, most have limited power to detect gender x treatment outcome.

Disulfiram

There is no systematic review and little indication from trials of disulfiram about which type of patient might be more likely to benefit from treatment.

7.4.1 Compliance and adherence

These are related to predictors of efficacy given that if a patient is not taking their medication as prescribed, then its effectiveness is likely to be reduced. Since acamprosate and naltrexone are generally well tolerated medications, problematic side-effects are unlikely to contribute significantly to reduced compliance.

This issue has only been studied with naltrexone where Rohsenow et al, (2000) found that compliance was better in those that believed that the medication would help them stay sober and was not predicted by demographic or pre-treatment alcohol use variables, commitment to abstinence or self-efficacy about abstinence.

For disulfiram, witnessing or supervision has been shown to be an important component of its effectiveness (Chick 1992, Sereny et al 1986). Those patients who might do better with

unsupervised disulfiram are older (Baekeland *et al*. 1971; Fuller *et al*. 1986); more socially stable (Fuller *et al* . 1986); impulsive (Banys 1988); and higher in motivation (Baekeland *et al*. 1971).

7.4.2 When to start pharmacological treatment

We are giving advice regarding prescribing these medications for relapse prevention and therefore patients should be abstinent from alcohol at the time of starting medication. All medications should be used as an adjunct to psychosocial treatment and not prescribed in isolation.

Acamprosate

The SPC recommends that "treatment with acamprosate should be initiated as soon as possible after the withdrawal period and should be maintained if the patient relapses". Advice to start as soon as possible was made since studies that allowed more than a couple of weeks after assisted withdrawal resulted in more patients drinking again before initiating acamprosate with consequent reduced efficacy. Given that individuals are at particularly high risk of relapse in the first few days and given that it takes about 5 days for acamprosate to achieve steady state levels, starting it as soon as possible seems sensible (Mason et al 2002).

In addition, there is evidence from preclinical models that acamprosate can reduce glutamatergic hyperactivity associated with alcohol withdrawal leading to reduced cellular damage (Spanagel et al, 1996; Qatari et al, 2001). Preliminary data from man suggests that acamprosate during withdrawal may also reduce hyperactivity and improve sleep (Boeijinga et al 2004; Staner et al, 2006). Consequently, some practitioners start the acamprosate for relapse prevention during or even before assisted withdrawal. Acamprosate has been started with assisted withdrawal with no reports of adverse events (Gual et al 2001; Kampan et al 2009). Acamprosate did not alter the course of alcohol withdrawal including CIWA-Ar score and amount of benzodiazepines taken. Unlike Gaul et al, (2001), Kampan et al, (2009) found that acamprosate started during assisted withdrawal was associated with poorer drinking outcomes compared to those who had placebo. However, Gaul et al, compared acamprosate with placebo for the entire treatment period whereas in Kampan et al, acamprosate was open label and without placebo in the relapse prevention phase.

Naltrexone

When using naltrexone for relapse prevention, patients should be abstinent. However, there is no information on the optimal time to start medication. Like acamprosate, it is safe to start naltrexone while patients are still drinking or during medically assisted withdrawal.

Disulfiram

Given the reaction between alcohol and disulfiram, treatment should only be started at least 24 hours after the last alcoholic drink (SPC).

7.4.3 How long to continue with pharmacological treatment

Most trials of medication are between 3 to 6 months and show efficacy. However many patients relapse within months to years but there is very limited evidence to guide how long medication should be continued. Patients who are doing well may be best advised to remain on medication for at least 6 months. However, some of these patients may feel confident enough to stop medication earlier. Alternatively some would prefer to stay on medication for longer; continuation beyond a year would need to be justified If a patient is not engaging with other aspects of treatment, for example, psychosocial and is drinking heavily, stopping the medication is appropriate until they engage with treatment. However if a patient is engaged but still drinking, a review of all of their treatment is indicated to assess whether this is optimal, including medication.

There is no evidence currently that long-term use of any of the relapse prevention pharmacotherapy incurs additional adverse consequences particularly when relapse to heavy drinking will be associated with morbidity and mortality. However, medication is ideally used as an adjunct to support engagement with psychosocial approaches to alter behaviour and attitudes to alcohol.

For acamprosate, Mann et al (2004) reported from their meta-analysis that the effect sizes increased with time (the effect sizes on abstinence at 3, 6, and 12 months were 1.33, 1.50, and 1.95 respectively. This suggests that a clinically relevant benefit of treatment may be observed as early as 3 months which gradually increases up to 1 year and possibly beyond. For naltrexone, there is evidence that its effects do not persist when it is stopped (O'Malley et al, 1996).

7.5 Assessment, monitoring and side effect profile

All patients for whom medication is being considered require medical review and assessment of their general fitness and their renal and liver function. Medication should be used as an adjunct to psychosocial treatment, so their engagement in psychosocial treatment should also be monitored. For a full description of the side-effects, contraindications and cautions, or interactions with other medications, prescribers must refer to the SPC or BNF.

Acamprosate

Acamprosate is a well tolerated medication with minimal side effects, contraindications or cautions associated with its use. The most common side effect is diarrhoea with abdominal pain, nausea, vomiting and pruritus also described. Its contraindications include pregnancy and breast feeding, renal insufficiency (serum creatinine >120 micromol/L) and severe hepatic failure (Childs- Pugh Classification C). There appear to be no drug interactions of clinical significance with alcohol.

Naltrexone

Naltrexone is also generally a well-tolerated medication with most trials reporting side effects similar to those reported with placebo or other drugs such as disulfiram or acamprosate. The most common side effects reported for naltrexone included nausea, headache, abdominal pain, reduced appetite and tiredness. However in some of these studies, 100mg/day rather than 50mg/day was used. Nausea has been reported more commonly at the start, particularly in female, lighter drinkers which can be minimised by starting at 25mg/day.

Since it is an opiate antagonist naltrexone cannot be used in those patients using opioid agonist drugs for analgesia. In addition, if analgesia is required in an emergency, non-opioid medication will be required since naltrexone blockade will last for 48-72 hours after taking the last tablet. It is therefore helpful that patients carry a card stating that they are taking naltrexone in case of such an emergency. If future analgesia is likely, for example in planned surgery, naltrexone is also therefore not ideal.

Hepatotoxicity was reported in association with use of naltrexone to treat obesity when high doses (>300/day) were used. Reviews of available data suggest and current US guidelines recommend that hepatic toxicity is very unlikely to occur with doses of at 50mg/day and that continued alcohol use is more likely than naltrexone to cause liver damage (FDA 'black box', accessed May 2010). Nevertheless, naltrexone should not be used in those with acute liver failure and caution is suggested when serum aminotransferases are 4 - 5 times above normal (Anton et al 2006; Kleber, 1985). Nevertheless, naltrexone has been used in patients with chronic hepatitis B and/or hepatitis C and no significant difference in LFT results with naltrexone at the recommended doses has been reported (Lozano Polo et al., 1997,

There is no consistent advice or evidence about monitoring of liver function tests for adverse effects on hepatic function. It is therefore important that the patient understands about the risk of hepatotoxicity and to stop taking naltrexone and promptly seek medical attention if they have any concerns about side effects or start to feel unwell. Deterioration in LFTs or signs of liver failure have not been widely reported and increases generally normalise on stopping naltrexone. Before ascribing any increases to naltrexone, review other possible contributors such as other medications – prescribed, over-the-counter, complementary treatments, resumption of drinking.

Disulfiram

Given the potential seriousness of the disulfiram – alcohol interaction in addition to the potential adverse effects of disulfiram alone, prescribing needs due care and consideration. Patients must be warned about and have capacity to understand the disulfiram-alcohol reaction and be made aware of the presence of alcohol in foodstuffs, perfumes, aerosols etc. In addition, they should not have consumed alcohol for at least 24 hours before staring disulfiram and should also be warned that a reaction with alcohol may be experienced for up to 7 days after their last tablet. The alcohol challenge test is no longer recommended (SPC; BNF). Fatal disulfiram-alcohol reactions have occured with high doses of the drug (> 1g/day) and were associated with cardiovascular complications such as hypotension or QTc on the ECG (Chick 1999; Kristenson, 1995). With the lower doses now prescribed more severe reactions after consuming alcohol are less likely to be seen (Malcolm et al 2008). Indeed, a survey of patients taking disulfiram found that for some an interaction only occurred when taking 800-1500mg/d (Brewer 1984).

The SPC or BNF lists several significant medical and psychiatric contraindications to its use, including cardiovascular problems, severe personality disorder, suicidal risk or psychosis, pregnancy, breast-feeding. Caution is also advised in the presence of renal failure, hepatic or respiratory disease, diabetes mellitus and epilepsy. Nevertheless, against this background there is some evidence of its prescribing in a broad range of conditions including possible contraindications such as those with psychotic disorders or cocaine dependence or on

methadone with no reports of significant adverse effects (Petrakis et al, 2005; Petrakis et al, 2000; Pani et al 2010).

Concerning the side effects of disulfiram alone, there are many fewer trials compared with acamprosate or naltrexone and some are older hence descriptions may be less comprehensive. Where reported, side effects and adverse events or reactions experienced include drowsiness, fatigue, abdominal pain, nausea, diarrhoea. Psychiatric problems were reported in some studies such as dysphoria or psychosis but the incidence was low. In newer trials comparing disulfiram with acamprosate or naltrexone, the reporting of side effects or adverse events is not dramatically different between the active drugs or placebo. Neuropathy has been reported by some but not all studies with onset commonly described over months to a year, though within days has been described (see Chick, 1999). From the Danish database, the estimate of rate of neuropathy was 1 in 15 000 patient years (Poulsen et al, 1992) though De Sousa et al, (2005) reported that 3 of the 50 (6%) patients taking disulfiram in their trial dropped out due to neuropathy.

Use of disulfiram may be associated with the development of an acute hepatitis, which can be fatal. The nature and exact incidence or prevalence of hepatotoxicity is unclear however it appears rare, for example, 30 reports of hepatitis in previous 40 years (Chick, 1999), 11 fatal liver reactions in 22 years (1968-1991). Based on estimates of number of patients taking disulfiram, the estimated the risk of dying from hepatotoxicity caused by disulfiram as 1:30 000 patients per year. However, some patients received disulfiram for nickel sensitivity who are reportedly at greater risk of hepatitis than those receiving disulfiram for alcoholism. Hepatotoxicity at 250mg/d after 13 days has been described though a review found disulfiram-related hepatitis starting 16-120 days later though in one case, jaundice appeared within 5 days after taking 1.5 – 2g/day ie up to 10x above recommended dose (Chick, 1999). Given the seriousness of hepatitis, a role for monitoring of liver function has been suggested but there is limited evidence to inform guidance. It is therefore important that the patient understands about the risk of hepatotoxicity and to stop taking disulfiram and promptly seek medical attention if they have any concerns about side effects or start to feel unwell.

Psychiatric complications such as psychosis or confusional states are potentially serious side-effects or adverse events and are more likely at higher doses (>500mg/day; Chick, 1999). The Danish and WHO databases report respectively 4% and 13% of all adverse effects of disulfiram were psychiatric (Poulsen et al, 1992). One clinical trial reported over 1 year in over 600 people reported no difference in psychiatric complications between those treated with disulfiram 250mg/d, or disulfiram 1mg/d or placebo with the incidence in disulfiram groups at 2.4% (Branchey et al, 1987). Nevertheless, in recent trials disulfiram has been used in patients with a variety of psychiatric comorbidities including depression, psychosis or schizophrenia without apparent psychiatric adverse events (see Chick, 19999; Petrakis et al, 2005; 2006). The rate and quality of adverse events with cocaine and disulfiram are similar to those seen with studies of alcohol dependence (Pettinati 2005; Carroll et al, 1998). Disulfiram has been also been used in patients maintained on methadone without reported serious adverse reactions (Ling, 1983)

The reader is directed to two comprehensive reviews regarding the safety of disulfiram by Chick, (1999) and Malcolm et al, (2008).

7.6 Health economic evidence

7.6.1 Systematic review

The literature search identified seven studies that assessed the cost-effectiveness of pharmacological agents for the maintenance phase of treatment of alcohol dependence (Annemans et al. 2000; Mortimer and Segal, 2005; Palmer et al. 2000; Rychlik et al. 2003; Schadlich & Brecht, 1998; Slattery et al. 2003; Zarkin et al. 2008). Full references, characteristics and results of all studies included in the economic review are presented in the form of evidence tables in the appendices.

Annemans and colleagues (2000) modelled the health care costs of acamprosate compared to no treatment in the prevention of alcoholic relapse over a 24-month time horizon. The patient population started the model following assisted withdrawal in an ambulatory state. Effectiveness data used to populate the model was sourced from several published and unpublished studies. A Belgian health payers' perspective was taken for the analysis. Therefore, only direct medical costs, relating to hospitalisations, psychiatric and GP consultations and medications, were included in the model. The total expected cost of the acamprosate strategy was €5,255 over the two-year time horizon compared with €5,783 in the no treatment arm. Therefore, despite the higher drug acquisition costs, acamprosate was shown to be a cost-saving intervention, in terms of reduced hospitalisations due to alcohol-related complications. The major limitation of the study was that it was a cost-analysis and did not consider the impact of the interventions on overall clinical effectiveness and patient quality of life. Furthermore, the study was from the Belgian health payer's perspective which may have limited applicability to the UK context.

The study by Mortimer and Segal (2005) conducted a model-based economic analysis of naltrexone plus counselling versus counselling alone amongst detoxified patients with a history of severe alcohol dependence. A lifetime horizon was used for all of the analysis. Clinical effectiveness was measured using QALYs which were calculated from disability weights derived from a single published source (Stouthard *et al.* 1997). Clinical effectiveness data were taken from published studies evaluating interventions targeting heavy drinkers at lower severity levels. These data were used to estimate how patients would progress between specific drinking states (problem, moderate or dependent) within the model. The authors did not specify the resource use and cost components included in the model within the article although an Australian health service perspective was adopted for the analysis. The results of the analysis suggested that naltrexone was cost-effective in comparison to standard care resulting in an ICER of $ AUD 12,966.

There are several limitations with the results of the study that reduce their applicability to any UK-based recommendations. Little explanation was given in the article as to how the clinical effectiveness data, which was taken from various sources, was used to inform the health states used in the economic models. The article did not specify the resource use and costs that were included in the analyses although a health perspective was used. The analysis used QALYs as the primary outcome measure, which allows for comparison across interventions, although again there was insufficient description of the utility weights that were applied to the health states within the model.

Palmer and colleagues (2000) modelled the lifetime cost-effectiveness of adjuvant acamprosate therapy, in conjunction with standard counselling therapy, compared with

standard counselling alone, in alcohol-dependent patients. The study population comprised men of an average age 41 years, who had been withdrawn from alcohol and had a mixture of alcohol-related complications. The model allowed patients to progress through various health states associated with important alcohol-related complications including liver disease, gastrointestinal disease, alcoholic cardiomyopathy and other complications. Clinical effectiveness data was sourced from 28 published studies that were not formally meta-analysed and authors' assumptions. The outcome measure used for the economic analysis was the number of life-years gained with adjuvant acamprosate over standard therapy. The perspective of the cost analysis was from German third-party payers. Costs, again reported in Deutschmarks, included those associated with drug acquisition and treatment of alcohol-related complications.

The results of the cost-effectiveness analysis showed that adjuvant acamprosate therapy was the dominant treatment strategy, resulting in lower costs (DM 48,245 versus DM 49,907) and greater benefits (15.9 versus 14.6 life-years gained) in comparison to standard therapy. Interpretation of the study results is subject to a number of methodological limitations. Firstly, a formal literature review was not undertaken in order to derive effectiveness estimates and no formal meta-analysis of summary data was performed, with the authors using data from studies selectively. Cost items used in the analysis were not reported adequately and unit costs and resources were not reported separately. Finally, as noted by the authors, no consideration was given to patients' quality of life in measuring the relative effectiveness of the treatments considered.

The objective of the study by Rychlik and colleagues (2003) was to compare the health care costs over one year of psychosocial rehabilitation support either alone or with adjuvant acamprosate treatment. The cost-effectiveness analysis was conducted alongside a prospective cohort study across 480 centres in the German primary care setting. Patients who fulfilled DSM-IV criteria for alcohol dependence were included in the study. The primary measure of clinical effectiveness in the study was abstinence rates after one year. The perspective of the study was from the German health insurance. Direct health care costs included medications, hospitalisations, outpatient care and diagnostic and laboratory tests. Total one-year costs were analysed according to both per-protocol (PPA) and intention-to-treat (ITT) due to the expected patient attrition. Within both analyses, the adjuvant acamprosate treatment resulted in lower costs (€1225-€1254 versus €1543-€1592) and higher rates of abstinence (32-23% versus 20-21%) in comparison to no adjuvant treatment. The results of the economic analysis may be of limited applicability to the UK setting due to the cohort study design, the study setting and the short time horizon, as well as the effectiveness measure used.

The study by Schadlich and Brecht (1998) was a model-based cost-effectiveness analysis comparing adjuvant acamprosate therapy (in addition to standard care) to standard care (placebo and counselling or psychotherapy) for alcohol dependence. The patient population were defined as being alcohol-dependent and abstinent from alcohol for up to 28 days prior to entering the study. Data were derived from a single double-blind RCT across 12 outpatient centres in Germany. The primary health outcome measure was the percentage of patients remaining abstinent at the end of 48-weeks of medication-free follow-up. Transition probabilities to target events within the model were elicited from clinical expert opinion. The outcome measures used in the cost-effectiveness analysis were cases of target events avoided including cases of alcoholic psychoses, alcohol dependence syndrome, acute alcoholic hepatitis and alcoholic liver cirrhosis. A German health care system perspective

was taken for the cost analysis. Costs (reported in Deutschmarks) included in the model related to hospital treatment, acamprosate acquisition and patient rehabilitation for target events.

The incremental cost-effectiveness ratio of acamprosate versus standard care was –DM 2,602 (range: -DM406 to –DM 8,830) per additional abstinent alcoholic, thus resulting in a net saving in terms of direct medical costs. The results of the study, based on a single RCT in Germany, are of limited relevance to the UK setting. No attempt was made to translate the intermediate outcome of abstinence into final outcomes such as QALYs, which are of greater relevance to decision-makers. Another limitation of the study was that resource use quantities were not reported separately from the costs. Costing was also performed retrospectively and was not based on the same patient sample that was used in the effectiveness analysis, thus limiting the study's internal validity.

The study by Slattery and colleagues (2003) developed an economic model to assess the cost-effectiveness of acamprosate, naltrexone and disulfiram compared to standard care within the Scottish health service setting. The population examined were 45-year old men and women with a diagnosis of alcohol dependence. The outcome measures used in the economic model were the number of patients who have abstained and number of patient deaths averted. The clinical effectiveness data was based on a methodologically diverse selection of trials which were not described within the study. Resource use involved in the pharmacological interventions included drug acquisition as well as outpatient and GP consultations. Costs were applied from Scottish health service estimates. Other health care costs included in the model were those associated with alcohol-related disease endpoints such as stroke, cancer, cirrhosis and alcohol-related psychoses. Costs were applied according to inpatient length of stay taken from Scottish medical records.

The total costs of pharmacological treatments and any disease endpoints for a hypothetical cohort of 1000 patients were compared with standard care over a 20 year time horizon, to determine any net health care cost savings. Acamprosate resulted in net savings of £68,928 whilst naltrexone and disulfiram resulted in net economic costs of £83,432 and £153,189 respectively in comparison to standard care amongst a hypothetical cohort of 1000 patients. Whilst the results of the study, based on a hypothetical cohort of patients within the Scottish health service, may be applicable to a UK setting, there are several problematic methodological issues with the study. First, the sources of the effectiveness data used in the model were not explicitly described by the authors who suggested that the data was taken from a methodologically diverse selection of trials, thus suggesting a high level of heterogeneity. Secondly, no attempt was made to translate intermediate clinical endpoints such as abstinence rates into Quality-Adjusted Life Years (QALYs), which are useful to decision makers when assessing the comparative cost-effectiveness of health care interventions.

Zarkin and colleagues (2008 evaluated the cost-effectiveness of the COMBINE study (Anton et al. 2006) interventions after 16 weeks of treatment. Within the study, patients with a primary diagnosis of alcohol dependence from across 11 US study sites were randomised to nine intervention groups. In eight groups, all patients received medical management (MM) and were randomised to receive naltrexone, acamprosate, combination (naltrexone and acamprosate) or placebo or combined behavioural intervention (CBI) in addition to naltrexone, acamprosate, combination or placebo. The ninth treatment group received CBI only (without MM). Three clinical measures were used in the economic analysis: percentage

of days abstinent, avoidance of heavy drinking and achieving a good clinical outcome (abstinent or moderate drinking without problems). Costs were analysed from the treatment provider perspective. Resource use included medications, staff time and laboratory tests.

Each intervention was ranked in increasing order of mean total cost for each of the three effectiveness measures. Only three interventions – MM and placebo, MM and naltrexone and naltrexone and acamprosate – were included in the final comparative analysis. This is because the other six interventions were dominated (resulting in higher mean costs but lower effectiveness) by the aforementioned interventions. The ICERs for the comparison of MM and naltrexone versus MM and placebo were $42 per percentage increase in days abstinent, $2,847 per patient avoiding heavy drinking and $1,690 per patient achieving a good clinical outcome. The ICERs for the comparison of naltrexone and acamprosate versus MM and naltrexone were $664 per percentage point increase in days abstinent, $8,095 per patient avoiding heavy drinking and $7,543 per patient achieving a good clinical outcome. This study is the only cost-effectiveness study reviewed that considered combinations of pharmacological and psychosocial interventions. However, there are a number of limitations when interpreting the results of the study. The cost analysis relied on the trial investigators judgement of best clinical practice which specifically relates to the US health care system and may not be generalisable to the UK health service. Interpretation of the results is further reduced by the short time horizon and the choice of outcome measures used in the analysis. Translation of intermediate outcomes such as rates of abstinence or moderate drinking into final outcomes such as QALYs would also be more helpful to decision-makers.

7.6.2 Health economic summary

Of the seven cost-effectiveness studies identified in the literature, four compared acamprosate to standard care (Annemans *et al.* 2000; Palmer *et al.* 2000; Rychlik *et al.* 2003; Schadlich and Brecht, 1998), one compared naltrexone to standard care (Mortimer and Segal, 2005), one study compared naltrexone, acamprosate and disulfiram to standard care (Slattery *et al.* 2003). The remaining study compared nine possible treatment combinations including naltrexone, acamprosate, combination (naltrexone and acamprosate) or placebo either alone or in combination with combined behavioural intervention. Only one study was UK-based (Zarkin *et al.* 2008) whilst the other studies were based in Belgian, German or US populations. Nearly all of the studies were model-based economic analyses except for Rychlik and colleagues (2003), which was a cohort-based study and Zarkin and colleagues (2008), which was based on the COMBINE RCT (Anton *et al*. 2006). Within nearly all of the studies, pharmacological treatments were provided as adjuvant treatments to standard care which differed across the studies considered.

In summary, the results suggested that acamprosate was either cost saving or the dominant treatment strategy (offering better outcomes at lower costs) in comparison to standard care. Naltrexone plus counselling was cost-effective compared to counselling alone in patients with a history of severe alcohol dependence (Mortimer and Segal, 2005). The one UK study showed that acamprosate resulted in significant health care cost savings whilst naltrexone and disulfiram resulted in significant net economic costs in comparison to standard care (Slattery et al. 2003). Zarkin and colleagues (2008) showed that naltrexone in addition to medical management and combination therapy (naltrexone plus acamprosate) were cost-effective over a 16-week period.

Providing an adequate summary of the health economics evidence presented here is difficult, due to the differences across the studies in terms of the comparator treatments

considered (i.e. definitions of 'standard care' differed across studies), study populations, costs and outcomes considered and other methodological differences. Overall, the f evidence reviewed is insufficient to support a single pharmacological treatment over any other.

7.7 Economic model

This section considers cost-effectiveness of pharmacological interventions as an adjunctive treatment for the prevention of relapse in people who are in recovery from alcohol dependence

7.7.1 Introduction

The systematic search of the economic literature identified a number of studies assessing the relative cost-effectiveness of pharmacological treatments, either alone or as an adjunct to psychological therapy, in the prevention of relapse in people who are in recovery from alcohol dependence. The studies varied in terms of both methodological quality and applicability to the UK context. The results overall were inconsistent and did not support one pharmacological therapy over another. Therefore, an economic model was developed in order to answer this question. The objective of the economic model was to explore the relative cost-effectiveness of pharmacological treatments for the prevention of relapse in people who are in recovery from alcohol dependence. The aim of the analysis was to reflect current UK clinical practice, using the most relevant and up-to-date information on costs and clinical outcomes. Details on the guideline systematic review of the economic literature on pharmacological interventions for relapse prevention are provided in Section 1.7.1.

7.7.2 Methods

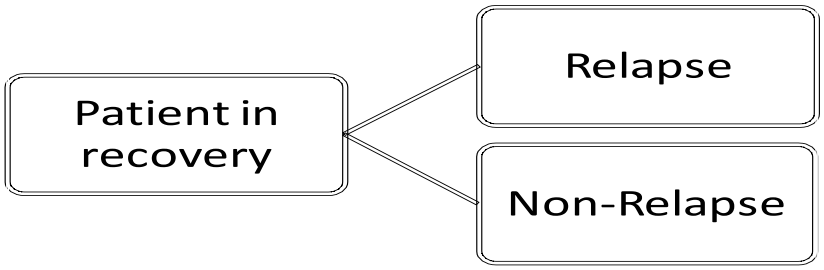
The choice of interventions assessed in the economic analysis was determined by the clinical data that was analysed within the guideline systematic literature review. Only pharmacological interventions licensed in the UK as first-line adjuvant treatments in the prevention of relapse in people in recovery from alcohol dependence were considered. As a result, both naltrexone and acamprosate were considered in the economic analysis. Disulfiram was not included in the economic analysis due to the scarcity of available clinical data, with only one study, comparing disulfiram with naltrexone, considering relapse to alcohol dependence as an outcome measure (De Sousa *et al.*, 2004). The GDG acknowledged that this was a limitation of the analysis, in terms of providing a comprehensive consideration of the relative cost-effectiveness of all available pharmacological interventions that currently exist within the UK.

7.7.3 Model Structure

A pragmatic decision model was constructed using Microsoft Excel 2007. Within the model a hypothetical cohort of 1000 patients who are in recovery from alcohol dependence can either relapse to heavy drinking (defined as 5+ drinks for males; 4+ drinks for females) or remain in recovery during a 12-month period. The structure of the decision tree is presented in Figure 3. The time horizon was chosen to reflect current UK guidance and recommendations, which recommend that patients should be maintained on pharmacological therapy for up to 12 months if patients are responding successfully to treatment. Three treatment groups were considered in the model: 1) Acamprosate and standard care; 2) Naltrexone and standard care and; 3) standard care alone. Standard care was defined as psychological therapy that patients would be receiving in order to prevent

relapse to heavy drinking. The psychological therapy would be delivered by a community nurse over the 12-month period.

Figure 9. Schematic of Model Structure



Costs and outcomes

The analysis adopted the perspective of the NHS and personal social services, as currently recommended by NICE (REF). Costs relating to drug acquisition, blood tests, psychological interventions, outpatient secondary care and primary care were considered in the analysis. The outcome measured was the Quality-adjusted Life Year (QALY).

Clinical input parameters and overview of methods of evidence synthesis

Clinical input parameters consisted of relapse rates associated with each intervention assessed: that is, naltrexone, acamprosate, or placebo. The economic analysis considered all relevant data reported in the studies included in the respective guideline systematic clinical review. To take all trial information into consideration, network (mixed treatment comparison) meta-analytic techniques were employed. Network meta-analysis is a generalisation of standard pair-wise meta-analysis for A versus B trials to data structures that include, for example, A versus B, B versus C and A versus C trials (Lu & Ades, 2004). A basic assumption of network meta-analysis is that direct and indirect evidence estimate the same parameter; in other words, the relative effect between A and B measured directly from a A versus B trial, is the same with the relative effect between A and B estimated indirectly from A versus C and B versus C trials. Network meta-analytic techniques strengthen inference concerning the relative effect of two treatments by including both direct and indirect comparisons between treatments and, at the same time, allow simultaneous inference on all treatments examined in the pair-wise trial comparisons while respecting randomisation (Lu & Ades, 2004; Caldwell et al., 2005). Simultaneous inference on the relative effect a number of treatments is possible provided that treatments participate in a single 'network of evidence', that is, every treatment is linked to at least one of the other treatments under assessment through direct or indirect comparisons.

Details on the methods and relapse data utilised in the network meta-analysis that was undertaken to estimate clinical input parameters for the economic analysis are presented in

Appendix 15. Table 15 provides the mean probability of relapse (as well as the respective 95% credible intervals) at one year of treatment for naltrexone, acamprosate and placebo, as estimated by network meta-analysis.

Table 102. Results of Network meta-analysis – Probability of relapse at 12 months

Treatment	Mean	Lower CrI	Upper CrI	Probability that treatment is best at reducing relapse over 12 months
Placebo	0.8956	0.5509	1.0	0
Naltrexone	0.8253	0.4095	0.9997	0.369
Acamprosate	0.8176	0.3894	0.9996	0.631

Relapse data

Data on rates of relapse to alcohol dependency were taken from 32 RCTs included in the guideline systematic review of pharmacological treatments for the prevention of relapse in people in recovery from alcohol dependence. All trials included pharmacological treatments as an adjunct to psychological treatment. The RCTs reported rates of relapse at three different time-points: 3 months (n=20), 6 months (n=9) and 12 months (n=3). Data were extracted from the guideline systematic review, which adopted an intention-to-treat analysis. Therefore, it was assumed that study participants who discontinued treatment early were likely to have an unfavourable outcome (i.e. relapse to alcohol dependence).The RCTs included in the MTC meta-analysis used different definitions of relapse and different baseline psychological therapies , a factor that may limit the generalisability of relapse rates across the studies considered. For studies that reported relapse rates at multiple timepoints, for example 3 and 6 months, relapse from the final endpoint, in this case 6 months, was used in the network meta-analysis .

Within the economic model, it was assumed that an equal proportion of patients within each treatment group would relapse at any monthly time interval (from 1 to 12 months). Monthly probabilities were calculated using the following formula (Miller & Homan, 1994):

$$\text{Probability in month } n = 1 - (1 - \text{Probability}_{\text{12 months}})^{n/12}$$

Where n =1,2,..,11

Utility data and estimation of Quality-adjusted Life Years

To express outcomes in the form of quality-adjusted life years (QALYs), the health states of the economic model were linked to appropriate utility scores. Utility scores represent the health-related quality of life (HRQoL) associated with specific health states on a scale from 0 (death) to 1 (perfect health). They are estimated using preference-based measures that capture people's preferences for the health states under consideration. The systematic search of the literature identified one study that reported utility scores for specific health states associated alcohol-related disorders (Kraemer et al., 2005).

The study by Kraemer and colleagues (2005) directly measured utility scores for a spectrum of alcohol-related health states using different methods of utility measurement including visual analogue scale (VAS), time trade-off (TTO) and standard gamble (SG) techniques. The study was based on a cross-sectional interview of 200 adults recruited from one clinic (n=100) and one community sample (n=100) in the US. Study subjects completed computerised versions of the utility rating exercises for their current health and 6 hypothetical alcohol-related health state scenarios presented in random order. Utility ratings were scaled from 0 to 1 and anchored by death (0) and perfect health (1). Table 16 summarises the mean utility scores for the six alcohol-related health states for the three techniques used. As the results in table show, for each of the techniques used, utility scores decreased as the severity of alcohol use increased.

Table 103. Mean utility scores for alcohol-related health states and utility measurement technique (adapted from Kraemer et al., 2005)

Alcohol-related health state scenario	VAS Mean (SD)	TTO Mean (SD)	SG Mean (SD)
Non-drinking	0.94 (0.09)	0.97 (0.13)	0.93 (0.15)
Safe drinking	0.85 (0.17)	0.94 (0.20)	0.88 (0.22)
At-risk drinking	0.72 (0.24)	0.84 (0.30)	0.82 (0.27)
Alcohol abuse	0.52 (0.23)	0.72 (0.35)	0.75 (0.29)
Alcohol dependence	0.36 (0.22)	0.54 (0.37)	0.67 (0.29)
Alcohol dependence, in recovery	0.71 (0.24)	0.86 (0.25)	0.83 (0.24)

NICE recommends the EQ-5D as the preferred measure of HRQoL in adults for use in cost-utility analyses. NICE also suggests that the measurement of changes in HRQoL should be reported directly from people with the condition examined, and the valuation of health states should be based on public preferences elicited using a choice-based method, such as TTO or SG, in a representative sample of the UK population. At the same time, it is recognised that EQ-5D utility scores may not be available or may be inappropriate for the condition or effects of treatment (NICE 2008a). The study by Kraemer and colleagues (2005) did not use the EQ-5D questionnaire to estimate utility scores and was based on a US population sample who did not experience the alcohol-related health states they were asked to rate. Furthermore, the patient sample was not randomly selected but were conveniently recruited either from clinic waiting rooms or self-selected within the community after responding to an advertisement. The low sample size (n=200) also limits the results of the study, contributing to the uncertainty around the mean utility score estimates. However, this was the only study identified in the literature review that applied utility scores to specific alcohol-related health states using appropriate measurement techniques (SG or TTO) as recommended by NICE.

The two health states of interest in the economic model were: a) in recovery from alcohol dependence and b) relapse to alcohol dependence. For these health states, the utility scores for the 'alcohol dependence' and 'alcohol dependence, in recovery' health states were chosen

from Kraemer and colleagues (2005). In the base-case analysis, the TTO utility scores were used whilst the SG utility scores were used in the sensitivity analysis.

Resource Use and Cost Data

Costs associated with pharmacological interventions for relapse prevention in people in recovery from alcohol dependence were calculated by combining resource use estimates with appropriate UK national unit costs. Costs relating to the interventions consisted of the relevant drug acquisition costs, psychological treatment, outpatient and primary care. People who relapsed to alcohol dependency were assumed to discontinue pharmacological and psychological treatment and incur other health care costs, as described below. Where necessary, costs were uplifted to 2009 prices using the Hospital and Community Health Services (HCHS) Pay and Prices Index (Curtis, 2009). Discounting was not required as the time horizon of the analysis was 12 months.

Drug acquisition costs

Drug acquisition costs were taken from the latest edition of the British National Formulary (British Medical Association & The Royal Pharmaceutical Society of Great Britain, 2010). The recommended daily dosage for acamprosate was 1998mg per day and for naltrexone was 50mg per day. The drug acquisition costs and monthly costs for both drugs included in the analysis are presented in Table 17

Table 104. Drug acquisition costs and estimated monthly costs of pharmacological interventions included in the economic model

Drug	Daily Dosage	Unit Cost (BNF 59, March 2010)	Monthly cost
Acamprosate	1998mg	Campral 333mg, 168-tab = £24	£26.10
Naltrexone	50mg	Nalorex 50mg, 28-tab = £22.79	£24.76

Other costs of patient management

Estimates on resource use associated with the psychological intervention, outpatient and primary care and blood laboratory tests were based on GDG expert opinion. It was assumed that patients in all three treatment arms would receive the same individual psychological intervention focused specifically on alcohol misuse (e.g. cognitive behavioural therapy, behavioural therapy or social network and environment based therapy) delivered by a practice nurse. It was assumed that each patient would receive one session per month or 12 sessions over the entire 12-month period if they did not relapse. It was assumed that patients in the three treatment groups would all require one initial 30-minute outpatient consultation with a consultant psychiatrist prior to starting treatment. Patients receiving adjuvant pharmacological interventions would require an additional two visits as part of their medical supervision. The second visit would be a 15-minute outpatient visit with a consultant psychiatrist and the third would be a GP consultation at the end of the 12-month period. At all three visits, it was assumed that patients would require blood tests (liver function test and urea and electrolytes) to monitor for any potential hepatotoxic effects. It was assumed that patients receiving standard care would not require any further monitoring. Further details of resource use and costs associated with patient management are provided in Table 18.

Table 105. Resource use over 12 months and unit costs associated with patient management for people in recovery from alcohol dependence

Service	Usage per person		Unit Cost (2008/09 Prices)	Source of unit costs; comments
	Pharmacological Intervention	Standard Care		
Psychological treatment	12	12	£88	Curtis, 2009; Nurse specialist (Community): £88 per hour of patient contact
Outpatient visit	2 (1 x 30 min; 1 x 15 min)	1 (1 x 30 min)	30 min: £161 15 min: £81	Curtis, 2009; Consultant Psychiatrist: £322 per hour of patient contact
GP visits	1	0	£35	Curtis, 2009; GP per surgery consultation lasting 11.7 minutes: £35
Laboratory blood tests (LFT; U&E)	3	0	LFT: £5.70 U&E: £4.63	Newcastle-upon-Tyne Hospitals NHS Foundation Trust – personal communication

Monthly cost of relapse to alcohol dependence

The monthly cost of relapse to alcohol dependence was based on estimates of the annual cost of alcohol misuse to the NHS in England by the Department of Health for 2007 (DoH, 2008). Cost components included hospital inpatient and day visits, outpatient visits, A&E and ambulance visits, primary care consultations and prescribed medications. The report estimated the total annual cost of alcohol harm to be £2.7bn in 2006/07 prices. These costs were based on the estimated number of higher-risk drinkers in England taken from mid-2006 estimates published by the ONS (ONS,2006). Higher-risk drinkers were defined as men who consumed 50 or more drinks per week and women who consumed 35 or more drinks per week. The total number of higher-risk drinkers in England in 2006 was estimated to be 2,653,545. To attribute a proportion of these NHS costs to dependent drinkers, required calculating the ratio of the estimated prevalence of alcohol dependence (5.9%) to the prevalence of hazardous drinking (24.2%) which were taken from the recent survey for adult psychiatric morbidity in England for 2007 (McManus *et al.*, 2009). Hazardous drinking was defined in the survey as a score of 8 or more on the AUDIT scale. It was assumed that this definition of hazardous drinking was equivalent to the definition of higher-risk drinkers in the Department of Health report (DoH, 2008). Multiplying this ratio by the total number of higher-risk drinkers produced an estimate of 646,939 dependent drinkers in England in 2006.

The survey also estimated the proportion of health care service use by people identified as dependent or hazardous drinkers (McManus *et al*., 2009). It was estimated that 10% of hazardous drinkers (but not dependent) and 21% of dependent drinkers used health care services in England during 2007. Assuming a ratio of 2.1, it was possible to estimate the total annual and monthly NHS costs attributable to people who relapse to alcohol dependency. The costs were inflated from 2006/07 prices using the HCHS index (Curtis, 2009). Total annual costs attributable to alcohol dependency were estimated at £1,800, giving a monthly cost of £150.

Data analysis and presentation of the results

Two methods were used to analyse the input parameter data and present the results of the economic analysis.

Firstly, a deterministic analysis was undertaken, where data are analysed as mean estimates and results are presented as mean total costs and QALYs associated with each treatment under consideration. Relative cost-effectiveness between alternative treatment options is estimated using incremental analysis: all options are first ranked from the most to the least effective; any options that are more costly than options that are more highly ranked are dominated (because they are also less effective) and excluded from further analysis. Subsequently, incremental cost-effectiveness ratios (ICERs) are calculated for all pairs of consecutive treatment options. ICERs express the additional cost pr additional unit of benefit associated with one treatment option relative to its comparator. Estimation of such a ratio allows for consideration of whether the additional benefit is worth the additional cost when choosing one treatment option over another. If the ICER for a given treatment option is higher than the ICER calculated for the previous intervention in the ranking of all interventions, this strategy is then excluded from further analysis on the basis of extended dominance. After excluding cases of extended dominance, ICERs are recalculated. The treatment option with the highest ICER below the cost-effectiveness threshold is the most cost-effective option.

Several sensitivity analyses were conducted to explore the impact of the uncertainty characterising model input parameters on the results of the deterministic analysis. The following scenarios were explored:

- Using utility scores from Kraemer and colleagues (2005) obtained from the standard gamble (SG) technique rather than time-trade-off. These mean utility scores were 0.67 for 'alcohol dependence' and 0.83 for 'alcohol dependence, in recovery'.
- Increase the level and intensity of patient monitoring whilst on pharmacological treatment so that patients in recovery receive 6 outpatient visits (5 with a consultant psychiatrist; 1 with a GP) over the 12 month period
- Vary the monthly cost of relapse, from £0 to £300

In addition to a deterministic analysis, a probabilistic analysis was also conducted. For this, model input parameters were assigned probability distributions (rather than expressed as point estimates), to reflect the uncertainty characterising the available clinical and cost data. Subsequently, 10,000 iterations were performed, each drawing random values from the distributions fitted to each model input parameter.

The probabilistic distribution of data on the probability of relapse over 12 months was based on the results of the MTC analysis with random values recorded for each of the 10,000 MTC

iterations performed in WinBUGS. In order to maintain the correlation between the posterior estimates for the probability of relapse over 12 months, data from each of the common MTC simulations for this parameter were exported jointly and fitted into the Excel file of the economic model where the probabilistic analysis was carried out.

To account for likely high skewness and variability, all monthly cost inputs, including the monthly cost of relapse, were assigned a gamma distribution based on an assumed standard error of 30% of the mean value used in the deterministic analysis. Utility estimates were assigned beta distributions, based on the standard errors around the mean values reported in the study by Kraemer and colleagues (2005).

Results of the probabilistic analysis are presented in the form of cost-effectiveness acceptability curves (CEACs), which demonstrate the probability of each treatment option being the most cost-effective among the strategies assessed at different levels of willingness-to-pay per unit of effectiveness (interpreted as different cost-effectiveness thresholds set by the decision-maker).

7.7.4 Results of economic model

Deterministic analysis

Table 76 provides mean costs and QALYs per 1,000 people for the interventions under consideration as well as the results of the incremental analyses. The interventions were ranked from highest to lowest in terms of the number of QALYs gained over 12 months. Acamprosate was associated with the highest costs and the highest number of QALYs whilst standard care was associated with the lowest costs and the lowest number of QALYs. The ICER for acamprosate versus standard care was £5,043 per QALY and was £1,899 per QALY for acamprosate versus naltrexone. The ICER for naltrexone versus standard care was £5,395 per QALY. All ICERs lie well below the cost-effectiveness threshold of £20,000-£30,000 per QALY currently set by NICE (NICE, 2008b).

Table 106. 12-month mean costs and QALYs and ICERs per 1,000 patients for pharmacological interventions used for relapse prevention in people in recovery from alcohol dependency

Treatment	QALYs	Costs	ICER per QALY
Acamprosate	683	£1,802,982	£5,043 vs Standard care £1,899 vs Naltrexone
Naltrexone	680	£1,797,737	£5,395 vs Standard care
Standard care	656	£1,664,382	-

Table 20 shows that the cost-effectiveness results were fairly robust under the scenarios explored in the sensitivity analysis. The ICERs for both pharmacological interventions compared to standard care increased to approximately £10,000 per QALY when utility scores estimated from the standard gamble technique were used. The ICERs for these comparisons increased to between £12,000-£13,000 per QALY when the intensity of patient monitoring was increased. When the monthly cost of relapse was £0, the ICERs for both interventions compared to standard care increased to approximately £10,000-£11,000 per

QALY. However, when the monthly cost of relapse was doubled to £300, both interventions dominated standard care, resulting in lower costs but higher QALYs over 12 months.

Table 107. Results of deterministic sensitivity analyses

Scenario tested	ICERs
1) Utility scores estimated from standard gamble instrument	1) Acamprosate vs Standard care: £10,087 2) Acamprosate vs Naltrexone: £3,798 3) Naltrexone vs Standard care: £10,789
2) Increased intensity of patient monitoring over 12-month period	1) Acamprosate vs Standard care: £12,270 2) Acamprosate vs Naltrexone: £13,323 3) Naltrexone vs Standard care: £10,789
3) Monthly cost of relapse is (a) £0; (b) £300	(a) 1) Acamprosate vs Standard care: £10,668 2) Acamprosate vs Naltrexone: £7,524 3) Naltrexone vs Standard care: £11,020 (b) 1) Acamprosate dominates Standard care 2) Acamprosate dominates Naltrexone 3) Naltrexone dominates Standard care

Probabilistic analysis

Results of the probabilistic analysis were very similar to those of the deterministic analysis – Acamprosate was associated with the highest costs and QALYs and standard care was associated with the lowest costs and QALYs. ICERs were very similar to those calculated in the deterministic analysis. Probabilistic analysis demonstrated that standard care had the highest probability of being cost-effective up to a willingness-to-pay (WTP) level of £6,000 per QALY. Above this figure, acamprosate had the highest probability of being the most cost-effective treatment option. Using the current threshold of £20,000-£30,000 per QALY set by NICE, the probability of acamprosate or naltrexone being the most-effective treatment option were approximately 52-53% and 44-45% respectively.

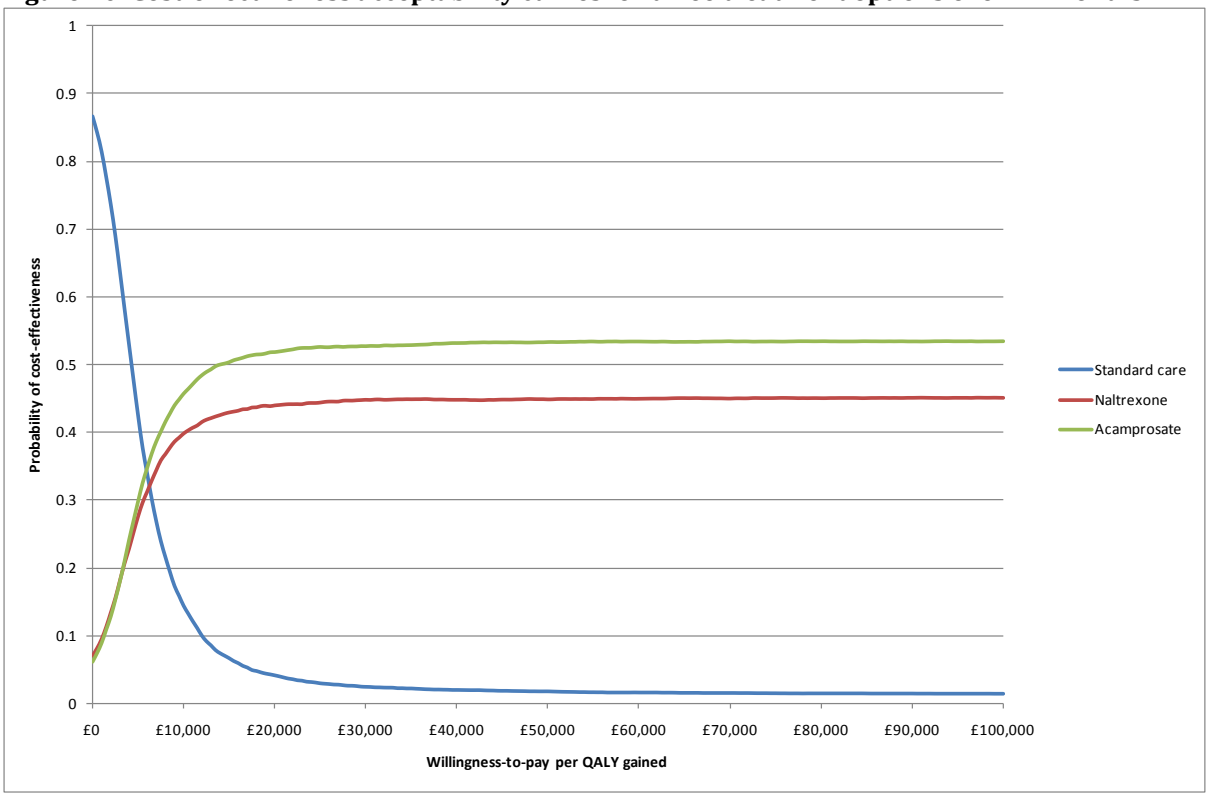
Figure 4 shows the CEACs generated for the three interventions considered whilst Table 21 shows the probabilities of each intervention being cost-effective at various levels of willingness-to-pay per QALY gained.

Table 108. Probability of each intervention being cost-effective at various levels of willingness-to-pay (WTP) per QALY gained

WTP	Acamprosate	Naltrexone	Standard care
£0	0.062	0.071	0.867

£10,000	0.457	0.399	0.144
£20,000	0.519	0.440	0.041
£30,000	0.527	0.449	0.024
£40,000	0.532	0.449	0.019
£50,000	0.533	0.449	0.018

Figure 10. Cost-effectiveness acceptability curves for three treatment options over 12 months



7.7.5 Discussion of economic model

The results of the economic analysis suggest that acamprosate is potentially the most cost-effective pharmacological treatment, when used as an adjunct to a psychological intervention, for relapse prevention in people in recovery from alcohol dependence. Given the uncertainty characterising the model input parameters, in particular the 12-month probability of relapse, the probability of either acamprosate or naltrexone being the most cost-effective option at the NICE cost-effectiveness threshold of £20,000, was 52% and 44% respectively.

A major limitation of the analysis was the exclusion of disulfiram, a pharmacological intervention that is currently licensed in the UK for the treatment of relapse prevention in people in recovery from alcohol dependence. Only one open-label RCT was identified in the systematic review that comparing disulfiram with naltrexone, considering relapse to alcohol dependence as an outcome measure (De Sousa *et al.*, 2004). Therefore, the GDG decided it would be inappropriate to include the results of this single study in the network meta-analysis.

Another possible limitation of the analysis is the relatively short time horizon of the economic model, although this reflected the time horizon of the RCTs that were included in

the systematic review and meta-analyses. Indeed, the majority of the trials included in the network meta-analysis measured rates of relapse up to 3 and 6 months with only three studies actually measuring rates of relapse up to 12 months follow-up. Ideally, a more comprehensive economic analysis would attempt to model the long-term cost-effectiveness of the three interventions, in terms of exploring the longer term impact of relapse prevention on future alcohol-related complications and survival. Earlier economic models have attempted to explore the longer-term cost-effectiveness of adjuvant pharmacological therapies over the patients' lifetime, by translating relapse to alcohol dependency into alcohol-related diseases including liver disease, cardiomyopathy, pancreatitis and alcoholic psychoses as well as alcohol-related mortality (Schadlich & Brecht, 1998; Palmer et al., 2000). However, these models required assumptions, often based on limited clinical evidence, about the longer-term prognosis of patients who relapsed to alcohol dependence.

The results of the network meta-analysis are undermined by the heterogeneity between studies in terms of the range of underlying psychological interventions and the study time horizons. All the studies included in the analysis were based on RCTs of pharmacological treatment or placebo as an adjunct to psychological interventions for the prevention of relapse. However, the RCTs included a wide range of psychological interventions including coping skills, counselling, brief CBI, MET and group therapies. The results of the meta-analyses presented here, including the network meta-analysis, assume that any differences in effectiveness are entirely explained by the adjuvant pharmacological interventions as opposed to the underlying psychological interventions. Whilst the economic model adopted a 12-month time horizon, the majority of the RCTs included in the network meta-analysis, were either 3 months (n=20) or 6 months (n=9) duration. The analysis attempted to extrapolate the majority of this data over a 12-month period. If the effectiveness of pharmacological interventions for relapse prevention actually declines over 12 months, the analysis may have over-estimated the cost-effectiveness of acamprosate or naltrexone.

The analysis was based on the perspective of the NHS and personal social services, as recommended by NICE. Costs associated with the interventions considered were estimated from national sources and GDG expert opinion. The results suggested that drug acquisition costs did not determine the relative cost-effectiveness of the three interventions. However, the results of the sensitivity analyses suggest that results may be sensitive to the intensity of patient monitoring (e.g. specialist visits, blood tests) which were estimated from GDG expert opinion and also the monthly costs of relapse to heavy drinking. However, within both sensitivity analyses, the ICERs for acamprosate and naltrexone were still well below the current NICE cost-effectiveness threshold.

7.7.6 Conclusions

The economic analysis undertaken for this guideline showed that both acamprosate and naltrexone may be potentially cost-effective pharmacological interventions for the prevention of relapse among people in recovery from alcohol dependence. The probability of either drug being the most cost-effective option at the NICE cost-effectiveness threshold of £20,000 was 52% and 44% respectively. However, further research is necessary to establish whether these pharmacological interventions are clinically and cost-effective in the longer term, in terms of preventing future alcohol-related diseases. Further clinical data, preferably based on double-blinded RCTs, is also needed to establish the clinical efficacy of disulfiram for relapse prevention.

7.7.7 From evidence to recommendations

The GDG reviewed the evidence for the clinical effectiveness and cost effectiveness of naltrexone and acamprosate for relapse prevention in individuals with alcohol dependence. A review was also carried out on the clinical effectiveness of disulfiram for relapse prevention in individuals with alcohol dependence, however as the evidence was much weaker, no cost effectiveness analyses could be conducted.

The clinical evidence for acamprosate suggested that individuals were likely to benefit from an increased chance of remaining completely abstinent from alcohol within the treatment and follow up periods. The amount of baseline drinking did not seem to have an impact on the effectiveness of acamprosate in preventing a lapse to drinking, but the studies included for the review on acamprosate was limited to studies where the participants were classed as at least moderately dependent. There was little evidence reviewed to show the effectiveness of acamprosate on harmful or mildly dependent drinkers. The studies reviewed mainly included a psychological treatment in addition to acamprosate. From the clinical evidence, the GDG decided to recommend acamprosate for relapse prevention in moderately to severely dependent drinkers combined with a psychological intervention as indicated in the license agreement.

The review of naltrexone for relapse prevention suggested a reduced likelihood of relapsing to heavy drinking in participants randomised to naltrexone instead of placebo. Further analysis also found that individuals drinking more at baseline were more likely to benefit from naltrexone in preventing relapse than individuals drinking lower baseline levels. The main evidence for naltrexone effectiveness was in reducing rates of relapse and reducing the amount of alcohol consumed, but the evidence for an effect on abstinence was more limited. The studies reviewed almost always included a psychological treatment in addition to naltrexone. From the clinical evidence, the GDG decided to recommend naltrexone for relapse prevention in moderately to severely dependent drinkers and as with acamprosate in combination with a psychological intervention.

For both acamprosate and naltraxone the GDG took the view that the psychological intervention provide in combination with either of the drugs should one of those identified as effective in Chapter 6 (i.e. BCT, CBT, BT or SNBT) as this was likely to bring the most benefit.

There was limited evidence comparing acamprosate against naltrexone for relapse prevention, and there was little evidence to suggest a benefit of one drug over the other. In studies comparing acamprosate plus naltrexone compared to acamprosate alone, naltrexone alone or placebo, there were no significant differences in outcomes in favour of the combination

The clinical evidence for disulfiram in relapse prevention was weaker than for acamprosate and naltrexone as most were open label, evidence from RCTs was even weaker. The double blind evidence for disulfiram versus placebo, suggested little benefit for disulfiram in maintaining abstinence or reducing drinking, however open-label studies showed a large effect in favour of disulfiram on these outcomes when comparing disulfiram to other pharmalogical agents.

Due to the weaker available evidence for disulfiram for relapse prevention and higher potential risks requiring monitoring, the GDG decided to recommend disulfiram as a

second-line treatment option for moderate to severe alcohol dependence for patients who are not suitable for acamprosate or naltrexone or have specified a preference for disulfiram and who aim abstain from alcohol. GDG consensus was that having the patient witnessed taking their disulfiram by a family member or carer would improve adherence to treatment.

7.7.8 Recommendations

Interventions for moderate and severe alcohol dependence

7.7.8.1 After a successful withdrawal consider offering oral naltrexone or acamprosate in combination with an individual psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment based therapies) focused specifically on alcohol misuse (see section 6.21.5). [KPI]

7.7.8.2 After a successful withdrawal consider offering oral naltrexone or acamprosate in combination with behavioural couples therapy to service users who have a regular partner and whose partner is willing to participate in treatment (see section 6.21.5).

7.7.8.3 After a successful withdrawal consider offering disulfiram in combination with a psychological intervention to service users who:

- want to achieve abstinence but for whom oral naltrexone and acamprosate are not suitable, **or**
- have specified a preference for disulfiram and understand the relative risks of taking the drug (see 7.7.8.12).

Delivering pharmacological interventions

7.7.8.4 Before starting treatment with acamprosate, naltrexone or disulfiram, undertake a comprehensive medical assessment (baseline urea and electrolytes and liver function tests including gamma glutamyl transpeptidase [GGT]). In particular, consider any contraindications or cautions (see the SPC or BNF).

Acamprosate

7.7.8.5 If using acamprosate, start treatment as soon as possible after assisted withdrawal and typically prescribe at a dose of 2 g (666 mg three times a day) unless the service user weighs less than 60 kg, and then a maximum of 1.332 mg should be prescribed per day. Acamprosate should:

- typically be prescribed for up to 12 months, or longer for those benefiting from the drug who want to continue with it
- be stopped if drinking persists 4–6 weeks after starting the drug.

7.7.8.6 Service users taking acamprosate should stay under medical supervision, at least monthly, for 6 months. Do not use blood tests routinely, but consider them to monitor for liver recovery and as a motivational aid for service users to show improvement.

Naltrexone

7.7.8.7 If using oral naltrexone, start treatment after assisted withdrawal and typically prescribe at a dose of 50 mg per day. Provide the service user with an information card about oral naltrexone and its impact on opioid-based analgesics, as part of a comprehensive medical assessment before prescribing. Oral naltrexone should:

- typically be prescribed for up to 12 months, or longer for those benefiting from the drug who want to continue with it
- be stopped if drinking persists 4–6 weeks after starting the drug.

7.7.8.8 Service users taking oral naltrexone should stay under medical supervision, at least monthly, for 6 months. Do not use blood tests routinely, but consider them to monitor for liver recovery and as a motivational aid for service users to show improvement. If the service user feels unwell advise them to stop the oral naltrexone immediately.

Disulfiram

7.7.8.9 If using disulfiram, start treatment at least 24 hours after the last alcoholic drink consumed. Typically prescribe at a dose of 200 mg per day.

7.7.8.10 Before starting treatment with disulfiram, carry out liver function tests, or urea and electrolyte tests, to assess for liver or renal impairment.

7.7.8.11 Make sure that service users taking disulfiram:

- stay under medical supervision, at least every 2 weeks for the first 2 months, then monthly for the following 4 months
- have a family member or carer oversee the administration of the drug.

7.7.8.12 Warn service users taking disulfiram, and their families or carers, about:

- the potential interaction between disulfiram and alcohol, and that alcohol may also be included in food, perfume, aerosol sprays, and so on
- the rapid and unpredictable onset of the rare complication of hepatotoxicity; advise service users that if they feel unwell or develop a fever or jaundice that they should stop taking disulfiram and seek urgent medical attention.

7.8 Other pharmacological interventions

Our systematic search identified a limited number of trials involving a range of medications for relapse prevention in alcohol dependence. We did not undertake a comprehensive assessment of all studies but used our expert opinion to focus on medications that we are

aware are being used in the UK, and/or those with encouraging evidence for their effectiveness. These are described below. The GDG concluded that no other medication warranted further consideration. For some, there were significant concerns about side-effect profiles or abuse liability, for example, GHB (Leone, 2010, Cochrane).

7.8.1 Extended release injectable naltrexone

In addition to oral naltrexone, an injectable formulation is available which has therefore an extended half-life and can overcome poor compliance.

In the US, naltrexone is also available in a once monthly extended release injectable formulation (380mg) and has been used by some in the UK. Two RCTs have been published regarding its efficacy and safety. Kranzler et al, (2004) studied a depot formulation in patients who were still drinking but wanted to stop and showed no efficacy on the primary outcome of reduced heavy drinking days. A longer time to first drink and a higher rate of abstinence were reported. The second study compared the 380mg injectable formulation with one containing 190mg over 6 months in still drinking alcoholics, and found reduced heavy drinking was seen in all groups but greatest in higher dose of naltrexone (Garbutt et al, 2005). In addition, greater efficacy was seen in men and in those that had been sober for a week before their injection. A post-hoc analysis revealed that naltrexone reduced alcohol consumption during holiday periods in the US, generally a time of great risk of relapse (Lapham et al, 2009).

Side effects or adverse effects of the extended injectable formulation are reported as similar to oral naltrexone and include abdominal pain, nausea, anorexia, dizziness although hepatic safety profile appears similar to placebo (Lucey et al, 2008). However, a greater number of injection site reactions with naltrexone have been reported which may need medical attention and be due to poor injection technique (Garbutt et al, 2009).

The initial evidence for the efficacy of injectable naltrexone is encouraging, particularly in those that may not be as compliant with oral naltrexone. However, at the current time there is not enough evidence to support its routine use.

7.8.2 Nalmefene

Like naltrexone, nalmefene is an opioid antagonist but with some kappa partial agonist activity or inverse agonist activity. It was initially proposed as a treatment for alcohol dependence since it has a longer half-life and was thought to have less risk of hepatoxicity then naltrexone. The first RCT in alcohol dependence reported significantly fewer relapses with nalmefene (20mg or 80mg/d; Mason et al 1999). However, a second multisite RCT comparing 5mg/d, 20mg/d with 40mg/d and placebo reported no efficacy for nalmefene (Anton et al 2004).

7.8.3 SSRIs

The efficacy of SSRIs in treating alcohol misuse without comorbid depression has been studied in three RCTs. They reported that SSRIs may have limited efficacy but importantly may also reduce the impact of psychosocial treatments in improving alcohol misuse in early-onset alcohol dependence. Kranzler et al, (1996) reported worse drinking outcomes in early-

onset or type B alcoholics on fluoxetine compared with placebo. Pettanti et al, (2000) found that sertraline had no effect in type B alcoholics, whilst improving outcomes in type A. Chick et al, (2000) reported that type II alcoholics, as defined by Cloninger's TPQ, had worse outcomes compared with those on placebo and type I alcoholics. Therefore, these three studies suggest that in the absence of a depressive disorder, SSRIs may weaken improvements in alcohol misuse.

One RCT has investigated whether combining naltrexone with sertraline is effective in improving drinking behaviour in native and non-native Alaskan Americans by randomising patients to daily naltrexone (50mg), sertraline (100 mg), naltrexone plus sertraline, or placebo (O'Malley et al 2002). Naltrexone significantly improved abstinence rates rather than reducing the risk of heavy drinking whilst sertraline had no further benefit.

Overall given the difficulties in making a diagnosis of depression in such a population, and the limited efficacy shown when comorbid depression is present, an SSRI may not be the most appropriate first line antidepressant to use in alcohol misuse.

7.8.4 Baclofen

Baclofen, a GABA-B agonist increases abstinence rates in patients with alcohol-related cirrhosis compared with placebo (Addolorato et al, 2008; 30mg/d; 12 weeks). It was well tolerated with little contribution to dropouts due to side effects; there were no adverse events reported. We are aware of a large RCT conducted in the US whose results are yet to be formally published but some of the data has been reported and suggest no efficacy for baclofen (Leggio et al, 2010). Key differences between the studies which are likely to increase likelihood of efficacy are: goal of abstinence, alcohol dependence requiring medically assisted withdrawal, higher anxiety levels.

7.8.5 Topiramate

Topiramate, an anticonvulsant with a rich pharmacology including increasing GABA and reducing glutamatergic activity, has been shown to reduce heavy drinking to promote abstinence (Johnson et al 2003; 2007). Unlike other trials of medication, the medication was started whilst the patients were still drinking but who were aiming for abstinence. Baltieri et al (2008) reported that patients receiving topiramate (up to 300mg/d) showed significantly better drinking outcomes early in the 12 week trial but not at 12 weeks compared with placebo. In addition, there were no significant differences in drinking outcomes between topiramate and naltrexone (50mg/d), though there were trends suggesting topiramate was the more effective. An issue for topiramate has been its side-effect profile such as paresthesia (up to 50%), dizziness, taste perversion, anorexia leading to weight loss, and difficulty with memory or concentration. In the largest multisite trial (Johnson et al 2007), 67 of 183 did not complete the study, of 34 had a limited adverse event (almost 20%). The dose is 25mg increasing to 300mg/d. Side effects are more pronounced and likely at higher doses and with more rapid titration.

Gabapentin and pregabalin

There is interest in both gabapentin and pregabalin for treating alcohol dependence since they have anticonvulsant and anxiolytic properties. They bind to calcium channels and reduce calcium currents resulting in reduced activity. In relapse prevention, gabapentin has been shown to increase time to heavy drinking and reduce alcohol craving (Brower et al,

2008; Furieri &Nakamura-Palacios, 2007; Mason et al, 2009). A small open study showed people who misused alcohol given pregabalin remained abstinent longer than those given naltrexone (Martinotti et al, 2008).

7.8.6 Clinical summary

A number of medications have been studied for their potential in preventing relapse in drinking behaviour. The evidence is clear that SSRIs do not improve drinking behaviour in non-depressed alcoholics and may worsen outcome. Only a few medications currently still show promise for potential routine use in the clinic including baclofen, topiramate, pregabalin, gabapentin, injectable naltrexone, nalmefene. There is evidence from a number of trials that these medications can reduce alcohol consumption and craving, and may reduce associated problems such as anxiety or insomnia. There are trials currently underway which will inform their potential role as adjunct to psychosocial approaches.

7.8.7 From evidence to recommendations

There is no convincing evidence to support the use of SSRIs in treating the alcohol problem and so their routine use is not recommended. There are some medications whose side-effect profile, for example, topiramate will require careful titration and monitoring. For others, their abuse liability, for example, GHB in absence of a clear advantage over safer medications is problematic and they are not recommended. Specialist prescribers should consider the latest evidence from trials of medication for relapse prevention and whether they might be helpful to a patient who is unable to take or has not responded to acamprosate, naltrexone or disulfiram.

7.8.8 Recommendations

7.8.8.1 Do not use antidepressants (including SSRIs) routinely for the treatment of alcohol misuse alone.

7.8.8.2 Do not use gammahydroxybutrate (GHB) for the treatment of alcohol misuse.

7.9 Pharmacotherapy for less severely dependent and non-dependent drinkers

In general, psychosocial approaches should be offered to all individuals who are problematic (or whatever terminology is) drinkers. For those for whom that has not worked or who are mildly dependent, medication may be considered. However the only medication that has been studied in this population is naltrexone since its underlying neurobiology is to reduce the positive reinforcement or pleasure associated with drinking. Whilst the majority of the trials included in our meta-analyses (see section xxx) required abstinence prior to starting naltrexone, when taken to reduce drinking patients are still drinking and the aim is that naltrexone reduces consumption.

Heinälä et al (2001) investigated whether naltrexone (50mg) started without assisted withdrawal in treatment seeking drinking alcoholics. They showed that in combination with coping skills but not supportive therapy, naltrexone reduced risk of relapse to heavy drinking but did not improve abstinence or time to first drink. In this study, abstinence was not emphasised as part of coping skills, but was in supportive therapy.

In less severely dependent and non-dependent drinkers, naltrexone (50mg/d) has been shown to reduce the likelihood of any drinking (Kranzler et al 2003). Interestingly, if they were taking medication (naltrexone or placebo) in a targeted manner ie when anticipating a high risk situation, greater reductions in heavy drinking days were seen compared with taking medication daily. A follow-up trial confirmed 'targeted' naltrexone reduced drinks/day, but only in men (Kranzler et al 2009). Notably both trials excluded people who had an unsuccessful attempt to reduce their drinking.

Leeman et al 2008 reported in pilot open study in heavy drinking young adults (18-25 yrs old) that targeted naltrexone (25mg in some) as an adjunct to counselling was well tolerated and reduced drinking suggesting that this might be a way forward to improve outcomes from counselling along.

Karhuvaara et al 2007 reported that in heavy drinkers having a problem controlling their drinking (some may have been dependent) that nalmefene (20mg/d) similarly reduced the number of heavy drinking days.

7.9.1 Clinical Summary

The evidence is limited to support the use of medication (specifically naltraxone) to reduce drinking in non-dependent or mild dependence and does not demonstrate equivalence with psychological interventions for this group. The GDG considered that given the limited evidence to support the use of naltraxone in reduce drinking in non-dependent or mild dependence that it should only be used where psychological interventions alone have been effective. It should be prescribed in conjunction with a psychological intervention.

7.10 Comorbidities

Individuals presenting for treatment with alcohol misuse may also present with features of other psychiatric disorders, most commonly anxiety or depression. For many, these symptoms will be closely linked with their alcohol misuse and lessen when drinking is reduced or stopped. For this reason, it is important to target their alcohol misuse rather than just starting treatment for a comorbid psychiatric disorder. Such comorbidity is associated with a poorer prognosis (Verheul et al, 1998; Bradizza et al, 2006; Mason & Lehert, 2010), to increased rates of relapse (Driessen *et al*, 2001), poorer medication compliance, lower treatment attendance rates and higher rates of self harm and suicidal behaviours (Martinez-Raga, *et al*, 2000).

There are a variety of treatment approaches for someone with comorbid alcohol dependence and psychiatric disorder but they all emphasise integrated treatment for both disorders. However, this is not always easy to achieve with thresholds for referral to 'addiction services' and 'psychiatric services' differing and lack of dedicated dual disorder service. In addition, addiction services vary in their psychiatric expertise. Provision varies considerably across the UK despite initiatives (Mental Health Policy-DH, 2002). The NICE guideline on psychosis with substance misuse will cover psychosis and substance misuse.

Psychological treatment approaches aimed at addressing Axis 1 and Axis 2 disorders have been increasingly developed but in many cases alcohol dependence remains a diagnosis of exclusion even though in many cases the comorbid psychopathology has preceded the diagnosis of alcohol dependence. On the basis of this, one might question whether or not

relapse rates could be influenced were treatment for co morbid disorders provided at the same time as those provided for alcohol dependence.

A systematic search and GDG knowledge was used to identify RCTs or meta-analyses of medication in non-psychotic psychiatric disorders. We did not undertake further synthesis of the data since, apart from in depression, the number, nature and quality of the studies did not permit this. Two meta-analyses of treating comorbidity of alcohol dependence and depression were drawn on. The expertise of the GDG was used to focus on key trials of relevance to current practice in the UK.

7.10.1 Alcohol misuse comorbid with a psychiatric disorder

This section considers two approaches for using pharmacotherapy and psychological interventions. First, its use for treating the alcohol misuse in the context of a non-psychotic psychiatric disorder and second for treating the comorbid psychiatric disorder.

Pharmacological interventions

There are limited studies of disulfiram, acamprosate or naltrexone in people with a psychiatric disorder and alcohol dependence. The largest randomised controlled study assessed the efficacy and safety of disulfiram and naltrexone in 254 people who misused alcohol with an Axis I psychiatric disorder (Petrakis et al, 2005). It was a heterogenous group with some individuals having more than one diagnosis. Individuals were randomised to naltrexone (50mg/d) or placebo (double-blind) but openly randomised to disulfiram (250mg/d) or nothing resulting in 4 groups: naltrexone alone, placebo alone, naltrexone+disulfiram, placebo +disulfiram. There was no overall advantage of one medication over the other, no advantage of the combination of both medications over placebo. However, the abstinence rate at 77% is very high.

A series of secondary analyses were then conducted to compare patients with and without particular axis 1 disorders within the group. In those with PTSD (37%) compared to those without (63%), either naltrexone or disulfiram alone or together improved alcohol outcomes (Petrakis et al 2006). PTSD symptoms also improved with those in disulfiram showing the greatest improvement. Those with PTSD were more likely to report GI, emotional or neurological side-effects. By comparison, the presence or absence of current depression did not influence outcomes (Petrakis et al, 2007).

In depressed alcoholics, Pettinati et al (2010) reported that the combination of sertraline and naltrexone resulted in better abstinence rates than with use of either medication alone or placebo (23.8%; $c2=12.9$, df=1, p=0.001). Notably there was no difference between the groups in improvements in depressive symptoms, though reported a trend favouring the combination (83% vs 58%; $c2= 6.1$, df=1, p=0.014).

Psychological interventions

Standard CBT was applied in four of the trials to treat alcohol dependence in addition to anxiety symptoms, panic disorder, insomnia and bipolar disorder. Cognitive Behaviour Therapy failed to demonstrate any significant improvement in relapse rates or percentage days abstinence with regard to alcohol use but did provide evidence of significant reduction in anxiety and avoidance symptoms (Schade *et al*, 2005), improved sleep (Currie *et al*, 2004), improved mood, medication compliance and attendance rates (Schmitz *et al*, 2002). One trial failed to provide any evidence that CBT reduced either anxiety symptoms or percentage

days abstinent when compared with treatment as usual (Bowen *et al*, 2000) although this was attributed, in part, to systemic resistance to introducing CBT into the setting and the subsequent poor planning associated with providing the intervention.

Integrated CBT, offered in two trials, also appeared to demonstrate limited effectiveness when applied to a population diagnosed with alcohol dependence and major depressive disorder when compared with Twelve Step Facilitation. One study (Glasner-Edwards *et al*, 2007) failed to demonstrate any improvement in mood or percent days abstinent amongst participants receiving ICBT compared to those receiving Twelve Step Facilitation.

A psychodynamic approach using Dynamic Deconstructive Therapy (Gregory *et al*, 2008) was applied in one of the trials to treat alcohol dependence or abuse with BPD. In this trial, DDP was compared with treatment as usual and results demonstrated a statistically significant improvement over time on each of the measures including parasuicide behaviours, a reduction in alcohol and drug use and fewer admissions to hospital. Integrated Group Therapy (Weiss *et al,* 2007)was applied in one trial where it was compared with Group Drug Counselling. Analysis indicated that participants undertaking the Integrated Group Therapy revealed significantly fewer days of substance use during treatment and at follow-up with decreased alcohol use accounting for most of the differences between the groups.

7.10.2 Treatment of the comorbid psychiatric disorder

This section focuses on the pharmacological and combined pharmacological and psychological interventions treatment of comorbid disorders. The issue of psychological interventions for alcohol misuse had been consider in relevant NICE guidance to which the reader is referred (NICE, 2011)

Depression

Several studies and trials have been performed to assess the efficacy of antidepressants in comorbid alcohol and depression, issues concerning methodology such as small numbers, unclear diagnoses, short treatment times, limit interpretation and translation to routine clinical practice. Two meta-analyses were undertaken of antidepressants in comorbid depression, one with substance misuse which included eight studies with alcohol dependence (Nunes & Levin, 2004) and a second that looked at the same studies in addition to one by another group and also examined SSRIs and 'other' antidepressants separately (Torrens et al, 2005).

In their review, Nunes and Levin (2004) included trials where patients met standard diagnostic criteria for current alcohol or other drug use and a current unipolar depressive disorder. The principal measure of effect size was the standardized difference between means on the Hamilton Depression Scale (HDS). Their meta-analysis reported that antidepressant medication exerts a modest (SMD 0.38 (95% confidence interval, 0.18-0.58) beneficial effect in reducing HDS score for patients with combined depressive- and substance-use disorders". Those with lower placebo response rates had larger effect sizes. In such studies, the depression was diagnosed after at least a week of abstinence. On the other hand, where studies included people whose depression was transient and/or directly related to their substance misuse, the placebo rate was high. This supports the widely held clinical practice of waiting to start an antidepressant once an individual is abstinent, but

suggests that a week rather than 2 to 3 weeks may be acceptable. In addition psychosocial interventions also contributed to reduced effect sizes which may have acted via improving mood directly or through reducing substance misuse. The overall effect size for improvements in substance misuse were small (0.25 (95% CI, 0.08-0.42)) with improvements observed in studies where the effect size in improving depression was > 0.5. Although it was noted that abstinence was rarely sustained. They concluded that an antidepressant "is not a stand-alone treatment, and concurrent therapy directly targeting the addiction is also indicated"

Torrens et al, (2005) included studies of alcohol dependence and depression where explicit diagnostic criteria and methods for assessing the presence of comorbid depression (major depression or dysthymia) were used. This meta-analysis also failed to find an overall effect of antidepressants on depressive symptoms. However there was a significant effect pooling the three studies using 'other antidepressants' (imipramine, desipramine, nefazodone; OR= 4.15 (95% CI, 1.35–12.75), whereas no significant effect was seen for SSRIs (OR= 1.85 (95% CI, 0.73–4.68)). However the meta-analysis revealed no significant effect on reduction in alcohol consumption. Torrens also note that cocaine misuse in addition to comorbid alcohol and depression, can result in greater levels of depression and poorer prognosis as reported in Cornelius et al, (1998).

Therefore, these two meta-analyses are in broad agreement that antidepressants do not reduce alcohol misuse. Whilst antidepressant effect is modest at best, waiting even for a week of abstinence to establish the diagnosis improves outcomes for depression. This is likely due to any transient depression due directly to their alcohol misuse or withdrawal period improving.

Nevertheless if an antidepressant is indicated, in view of several trials showing no or limited efficacy with SSRIs as opposed to more positive results with mixed noradrenergic-serotonergic antidepressants, choosing ones with similar pharmacology is worth considering. Such antidepressants include tricylics but these may not be appropriate due to the risk of cardiotoxicity with alcohol, particularly in overdose. Newer mixed noradrenergic-serotonergic antidepressant drugs include mirtazapine. Unfortunately, there are only two preliminary studies investigating mirtazapine in comorbid alcoholism and depression. An open label naturalistic study showed that mirtazapine (dose ranged on average from 17mg/d to 23mg/d) was associated with improved mood and craving for alcohol (Yoon et al 2006). A randomised double-blind trial comparing mirtazapine (average dose 45mg/d) with amitriptyline (average dose 125mg/d) found that both drugs improved mood and alcohol craving with no difference between them (Altintoprak et al 2008).

Anxiety

Despite how commonly alcoholism and anxiety are linked, few studies have investigated how to manage this challenging comorbidity. A comprehensive assessment is required to define how alcohol and anxiety are related. An assisted withdrawal is often required and a longer 'tail' of a benzodiazepine may be given to manage their anxiety initially. It is reported that anxiety may take up to 6 –8 weeks to reduce after stopping drinking. Benzodiazepines are also indicated for treating anxiety but due to concerns about vulnerability to dependence (see section 1.10.2), their use needs careful consideration.

A series of studies from the same group have shown that an SSRI, paroxetine, is safe and well tolerated in people with alcohol misuse or dependence who may be still drinking and that it can significantly reduce social phobia compared to placebo (Randall et al, 2001; Book et al 2008; Thomas et al, 2008). However, improvements in alcohol outcomes were either not reported or were no different to those in the placebo group and nonsignificant during the study. For instance, Thomas et al, (2008) found that although paroxetine successfully treated comorbid social anxiety, their drinking overall did not improve though their drinking to cope with anxiety reduced. This emphasises that improving a comorbid disorder does not necessarily lead to improved drinking and as with for depression, alcohol focussed treatment must be delivered.

In another study, Randall et al (2001) investigated how simultaneous CBT treatment of alcohol misuse and social anxiety disorder compared with CBT treatment of alcoholism alone. Although drinking outcomes improved in both groups, those who received simultaneous treatment showed less improvement. Notably, social anxiety showed equal improvement in both groups. Similarly, an RCT in abstinent alcohol dependent individuals with either social phobia or agoraphobia who received either intensive relapse prevention for alcoholism with or without a CBT anxiety programme plus an SSRI (fluvoxamine) was available if wanted resulted in reduced anxiety symptoms but no impact on alcohol outcomes (Schade et al, 2005).

A meta-analysis of five studies of buspirone in alcoholism and anxiety concluded that anxiety improved with buspirone, but not alcohol consumption (Malec et al, 2007).

Benzodiazepines are used in the treatment of anxiety, however their use in people with alcohol problems is generally regarded as inappropriate. Clearly any such prescribing should be done with due consideration and monitoring however their use may be the best option if their anxiety improves without adverse consequences on their drinking. Mueller et al (2005) monitored the clinical course of patients in their anxiety research programme over 12 years and reported that there little misuse of benzodiazepines in those who have coexisting anxiety disorders and alcohol use disorders.

PTSD

PTSD is a commonly associated with alcohol misuse (see NICE (2005)). Longitudinal studies have shown that PTSD often predates alcohol misuse. Treatment for their PTSD can improve their substance misuse but once dependent, this will need to be treated before the patient can benefit from trauma-focused psychological treatments.

In a placebo-controlled trial of sertraline treatment of PTSD in individuals with comorbid alcohol dependence, sertraline improved symptoms of PTSD but decreased alcohol use in only a small subset of the study population (Brady et al., 2003). A more recent, placebo-controlled trial compared sertraline with placebo in the treatment of PTSD with co-occurring alcohol dependence (Brady et al 2005). Both groups demonstrated a significant decrease in alcohol use. Cluster analysis revealed that sertraline was better in those less severely dependent with early onset PTSD whilst those more severely dependent with later onset PTSD improved more with placebo. Closer examination of this trial revealed that alcohol consumption tended to start improving before or together with improvements in PTSD symptoms (Back et al 2006). They concluded that PTSD symptoms could have a strong impact on alcohol consumption and that PTSD treatment may be important to optimize outcomes for those comorbid for PTSD and alcohol dependence.

ADHD

The prevalence of alcohol misuse is higher in adults with ADHD than general population (Upadhyaya, 2007). Some features of ADHD are similar to those seen in fetal alcohol syndrome or spectrum disorders (FASD) and a comprehensive history should be taken to establish whether FASD is implicated. There are treatment and prognostic implications since those with FASD may respond differently to psychostimulants (O'Malley & Nanson, 2002) Whilst psychotimulants are the first line treatment for ADHD, their use in people with comorbid substance misuse is complex and either medication must be adequately supervised or an alternative found (see NICE, ADHD guidelines).

A 3 month double-blind placebo controlled RCT in adults with ADHD and alcohol use disorders reported improved ADHD symptoms from atomoxetine compared with placebo (Wilens et al 2008). However there were inconsistent effects on alcohol with reduced cumulative number of heavy drinking days but not increased time to relapse of heavy drinking.

7.10.3 Comorbid alcohol and drug misuse

This section covers pharmacotherapy of comorbidities where it either plays a significant role in management e.g, opioid dependence, or where pharmacotherapy has not been shown to be generally efficacious e.g, cocaine. It does not cover comorbidity with drugs of abuse where psychosocial approaches are preferable and pharmacotherapy does not play a significant role, for example, cannabis, ecstasy, ketamine.

Comorbid opioid and alcohol dependence

The reader is referred to the NICE guideline (2008a; 2008b) and Orange Guideline (DH, 2009) for guidance about managing opiate dependence and alcohol misuse. Optimisation of their substitute pharmacotherapy is important though it does not seem to influence drinking whether this is with buprenorphine or methadone. However, it is recommended that drug misusers who are also misusing alcohol should be offered standard alcohol treatments such as assisted withdrawal and alcohol-focused psychosocial therapies as appropriate.

Concerning pharmacotherapy for relapse prevention, naltrexone is not an option unless the individual is also abstinent from opioids. There is a small study of disulfiram in methadone maintained opioid addicts with problem drinking (Ling et al, 1983). No benefit of disulfiram was shown but also no adverse events were reported.

There are no published studies of acamprosate in opioid dependent populations. Given its good tolerability and safety, there is no reason why acamprosate cannot be used to support abstinence from alcohol after the appropriate medical assessment.

The paucity of trials investigating pharmacotherapeutic options to reduce alcohol misuse in opioid dependence is notable.

Comorbid cocaine and alcohol misuse

If cocaine is taken with alcohol, cocaethylene is produced which has a longer half-life than cocaine leading to enhanced effects. For instance, taken together cocaine and alcohol can

result in greater euphoria and increased heart rate compared to either drug alone (McCance-Katz et al, 1993 & 1995; Pennings et al, 2002).

The reader is directed to NICE guidance regarding psychosocial management of cocaine (NICE, 2007) since there is limited evidence for efficacy of a broad range of pharmacotherapeutic approaches for cocaine misuse alone. There have been several trials of naltrexone and disulfiram in comorbid alcohol and cocaine misuse but none with acamprosate.

Naltrexone does not appear to significantly improve outcomes when added to psychosocial approaches for cocaine or alcohol in cormorbid dependence (Schmitz et al 2004 & 2009; Pettinati et al, 2008). A series of studies have reported that disulfiram in comorbid cocaine and alcohol dependence results in better retention in treatment and longer abstinence from cocaine or alcohol (Carroll et al, 1998; 2000). Although the initial rationale was that by reducing alcohol consumption, cocaine use would also reduce, effects on cocaine now appear somewhat independent of changes in alcohol consumption (Carroll et al, 2004).

Cormorbid nicotine and alcohol dependence

It is fair to say that conventional wisdom has been to 'give up one vice at a time'. The idea of stopping smoking and drinking alcohol concurrently has often not been encouraged. In addition, it is our clinical impression that most patients do not want to consider quitting smoking until they have achieved some sobriety. However, it is likely that since the smoking bans came into place and support to stop smoking has become more available, more alcoholics will be interested in stopping smoking.

Those who have achieved long-term abstinence from alcohol, have similar quit rates to non-alcoholics (Hughes & Kalman, 2006; Kalman et al 2010). However, the length of abstinence does influence outcome with quitting smoking less likely in those in the early months of sobriety. Two randomised trials comparing concurrent with sequential treatment for alcohol and nicotine have been conducted. Joseph et al, (2004) compared giving smoking cessation treatment concurrently with an intensive programme for alcohol versus delaying the smoking cessation programme for 6 months. Whilst there was no difference in smoking cessation (~16%) between the groups, those who received the delayed intervention had higher rates of alcohol abstinence. However, there were no group differences in time to first relapse or number of days drinking in previous 6 months. Kalman et al, (2001) showed higher (19% vs 8%), but nonsignifcant, smoking quit rates in alcoholics receiving concurrent smoking cessation interventions compared to those who received this intervention at 6 weeks. Regarding drinking outcomes, those who had the later smoking cessation intervention had greater relapse rates.

A meta-analysis of RCTs of smoking cessation intervention for people in treatment for or recovery from an addiction, 5 of which were primarily alcohol, concluded that there was no detrimental effect on substance use outcomes from combined treatment (Prochaska et al, 2004). Indeed smoking cessation interventions during substance misuse treatment seemed to improve rather than compromise long-term sobriety. Regarding smoking cessation, short-term abstinence looked promising but this was not sustained in the longer-term.

Therefore evidence does not strongly support a particular approach or time for quitting smoking, but it is very important that it is considered as part of their care plan. Some

suggest whilst it is difficult to know conclusively that concurrent treatment should be avoided, this is a possibility and therefore only offered if the patient requests it (Kodl et al, 2006). Others cite that there is a wealth of evidence to suggest that treatment for smoking does not interfere with recovery in substance misuse (Fiore et al, 2008).

Concerning pharmacotherapeutic strategies, (Kalman et al, 2010) reviewed all studies which include those both in alcohol abstinence and when still drinking. They suggest that more intensive treatment is needed since standard (weekly counselling plus 21-mg patch for 8–12 weeks) treatment does not produce good results in drinking or recently sober alcoholics. In the absence of trials, standard protocols can be followed however a comprehensive medical assessment of any individual is needed given contraindications/cautions for some pharmacotherapy that might be relevant in alcoholism eg bupropion – history of seizures, varenicline – close monitoring in those with psychiatric disorders (see BNF, SPC).

A full assessment of smoking and their attitudes to changing their smoking behaviour and cessation should be explored at initiation and throughout treatment. For management of smoking cessation, please refer to the relevant NICE guidance about services, pharmacotherapeutic and behavioural/psychological approaches.

7.10.4 Evidence summary for comorbidities

Whilst comorbidity with a psychiatric disorder or another substance is common, there were few studies investigating pharmacological treatments. Some studies were older and therefore diagnostic criteria differed from those undertaken more recently; a proportion were of poor quality with small numbers.

In the RCTs that included patients with alcohol dependence and a variety of psychiatric disorders, no benefit of medication (naltrexone, disulfiram or combination) on improving alcohol consumption was found. However, the abstinent rate was much higher than would normally be seen in routine clinical practice. Secondary analyses reported no advantage of medication in improving alcohol consumption when comparing those currently depressed vs non-depressed but did show a beneficial effect in those with PTSD compared to those without. This emphasises the importance of treatment targeted at their alcohol misuse is key rather than hoping an antidepressant will improve their drinking by improving mood. Whilst there were no adverse effects on their psychiatric disorder, no significant benefits were apparent either. A more recent trial in cormorbid alcohol dependence and depression found that naltrexone but not sertraline improved alcohol outcomes with mood similarly improving in all groups. There are no studies of acamprosate in comorbidity however it could be considered given its good safety profile. There is little consistent evidence for the use of psychological interventions for the treatment of alcohol dependence in people with comorbid psychiatric disorders. Where evidence of benefit from some psychological interventions was identified it was often from mixed drug and alcohol populations from small single studies and was not judged sufficient evidence on which to base a recommendation.

The two meta-analyses of treatment of comorbid depression broadly came to the same conclusion that antidepressants had a modest to no effect on improving depressive symptoms in those who are not at least a week sober. The effect of the antidepressant on alcohol use was also of limited benefit and where there was some, abstinence was not sustained. In those with severe depression, antidepressants may improve mood, but alcohol-focussed treatment is still required. There is little evidence to suggest which antidepressant

is best, although one meta-analysis suggested that SSRI were less effective than those with a mixed serotonergic-noradrenergic pharmacology. However some of these medications also carry adverse safety profiles with alcohol and there is insufficient evidence about the newer antidepressants. In the few studies in those with an anxiety disorder, whilst antidepressant medication may improve anxiety symptoms this was not associated with a beneficial effect on alcohol consumption. The evidence for those with either comorbid depression or anxiety suggests that focusing on managing their alcohol misuse at the start is key since whilst medication may help their anxiety or depression, improvements in their alcohol misuse will not necessarily follow.

There were only a few studies about the role of pharmacotherapy in those with alcohol and illicit drug misuse. Treatment of their illicit drug misuse must be optimised using psychosocial and/or pharmacological approaches as appropriate whilst monitoring the effect this has on their alcohol consumption to ensure alcohol does not substitute for reducing illicit drug misuse. Their alcohol misuse must also be specifically addressed. Many individuals with alcohol misuse smoke heavily and should be offered support to stop. There is limited evidence to suggest whether alcohol and nicotine should be given up simultaneously or sequentially therefore patient preference should guide the decision.

7.10.5 Evidence to Recommendations

The GDG noted that symptoms of anxiety and depression are common in people with harmful alcohol use or alcohol dependence. However, for many people the symptoms remit once abstinence or a significant reduction in alcohol consumption has been achieved. In addition, treatment for comorbid disorders (depression and anxiety) whilst people are consuming significant levels of alcohol does not appear to be effective. However, a number of patients have comorbid disorders which do not remit when alcohol consumption is reduced. The GDG therefore recommend that the first step in treating some presenting with alcohol misuse and comobrid depression/anxiety is to first treat the alcohol problem. Given the presence a comorbid disorder following a reduction in alcohol consumption is associated with a poorer long-term prognosis, 3-4 weeks after abstinence is achieved an assessment of the presence and need for treatment for any comorbid depression or anxiety should be considered. Some people with depressive disorders will require immediate treatment for example those at significant risk of suicide, and the recommendations below should not on any way stand in way of immediate treatment being provided in such a situation. In reviewing evidence for comorbid disorders the GDG did not find any treatment strategies or adjustments that should be made because of the comorbid problem and in view of this decided to refer to the relevant NICE guidelines (see NICE guideline on common mental health problems; NICE, 2011b). Given high prevalence of smoking in people with alcohol related problems the GDG thought it was important to emphasise need for effective treatment in this population. For people with comorbid drug and alcohol misuse and psychotic disorders see NICE guideline on (NICE, 2011b)

7.10.6 Recommendations

7.10.6.1 For people who misuse alcohol and have comorbid depression or anxiety disorders, treat the alcohol misuse first as this may lead to significant improvement in the depression and anxiety. If depression or anxiety continues after 3 to 4 weeks of abstinence from alcohol, undertake an assessment of the depression or anxiety and

consider referral and treatment in line with the relevant NICE guideline for the particular disorder. [KPI]

7.10.6.2 Refer people who misuse alcohol and have a significant comorbid mental disorder, and those assessed to be at high risk of suicide, to a psychiatrist to make sure that effective assessment, treatment and risk-management plans are in place.

7.10.6.3 For the treatment of comorbid mental health disorders consult the relevant NICE guideline for the particular disorder and be aware that:

- for alcohol misuse comorbid with opioid, cocaine or benzodiazepine misuse both conditions should be actively treated.
- service users who have been dependent on alcohol will need to be abstinent, or have very significantly reduced their drinking, to benefit from a psychological intervention for comorbid mental health disorders.

7.10.6.4 For comorbid alcohol and nicotine dependence, encourage service users to stop smoking and refer to the 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health guidance 1).

7.10.7 Research recommendation

7.10.7.1 For people who are dependent on alcohol, which medication is most likely to improve concordance and thereby promote abstinence and prevent relapse?

This question should be answered by: a) an initial development phase in which a series of qualitative and quantitative reasons for non-compliance/discontinuing drugs used in the treatment of alcohol are explored; b) a series of pilot trials of novel interventions developed to address the problems identified in (a) undertaken to support the design of a series of definitive trials; c) a (series of) definitive trial(s) of the interventions that were successfully piloted in (b) using a randomised controlled design that reports short-term (e.g. 3 months) and longer-term (e.g. 18 months) outcomes. The outcomes chosen should reflect both observer and service user-rated assessments of improvement and the acceptability of the intervention. Each individual study needs to be large enough to determine the presence or absence of clinically important effects, and mediators and moderators of response should be investigated.

Why this is important

Rates of attrition in trials of drugs to promote abstinence and prevent relapse in alcohol dependence is high (often over 65%), yet despite this the interventions are still clinically and cost effective. Retaining more service users in treatment could further significantly improve outcomes for people who misuse alcohol and ensure increased effectiveness in the use of health service resources. The outcome of these studies may also help improve clinical confidence in the use of effective medications (such as acamprosate and naltraxone), which despite their cost effectiveness are currently offered to only a minority of service users who

are eligible in the UK healthcare system. Overall, the results of these studies will have important implications for the provision of pharmacological treatment for alcohol misuse in the NHS.

7.11 Wernicke-Korsakoff Syndrome

The following section draws on the review of Wernicke-Korsakoff syndrome (WKS) is developed as part of the NICE (2010b) guideline on the management of alcohol-related physical complications including the management of acute withdrawal and similarly the GDG failed to identify in any of its searches any evidence for specific interventions in WKS beyond prevention strategies using thiamine which are covered in the other guideline (NICE, 2010b). The GDG therefore adopted a consensus based approach to the development of the recommendations for this guideline.

Wernicke's encephalopathy (WE) is traditionally thought of as a disorder of acute onset characterized by nystagmus, abducent and conjugate gaze palsies, ataxia of gait, and a global confusional state, occurring together or in various combinations (Victor et al., 1989). Wernicke first described the disorder in 1881 and the symptoms he recorded included disturbances of eye movement, ataxia of gait, polyneuropathy, and mental changes including apathy, decreased attention span and disorientation in time and space. Work by Alexander (1939) and then Jolliffe (1941) established that a deficiency in thiamine (vitamin B1) was central to causation and potential treatment of the disorder (Lishman, 1998). Korsakoff gave the first comprehensive account of the amnestic syndrome now known as Korsakoff psychosis (KP) in 1887 which includes features such as delirium, but is characterised by recent memory loss with confabulation but with relative preservation of other intellectual functions. More recent work has highlighted a retrograde memory impairment with a 'temporal gradient', such that earlier memories are recalled better than more recent ones (Kopelman et al., 2009). The two disorders were brought together by Victor and colleagues in 1971 (Victor et al., 1971) and Wernicke-Korsakoff syndrome (WKS) is now considered to be a unitary disorder comprising acute WE which proceeds in a proportion of cases to KP. A major complicating factor is that the pathology of WE may not be associated with the classical clinical triad (see above) in up to 90% of patients (Harper et al., 1986). Therefore, it has been suggested that a presumptive diagnosis of WE should be made for any patient with a history of alcohol dependence who may be at risk. This includes anyone showing evidence of ophthalmoplegia, ataxia, acute confusion, memory disturbance, unexplained hypotension, hypothermia, coma, or unconsciousness (Cook 2000). Untreated, WE leads to death in up to 20% of cases (Harper, 1979, Harper et al., 1986), or KP in up to 85% of the survivors. A quarter of the latter group may then require long-term institutionalization (Victor et al., 1989). Furthermore, the incidence of KP has been reported to be rising in some parts of the UK (Ramayya and Jauhar, 1997). For the reasons mentioned above it is probable that WE is under-diagnosed and inadequately treated in hospital, let alone in the community (Thomson and Marshall, 2006). We therefore do not know how often patients with alcohol dependence in the community unnecessarily suffer brain damage.

Cognitive impairment is common in people with chronic alcohol use disorders, with between 50% and 80% experiencing mild to severe cognitive deficits (Bates et al., 2002). The clinical and neuropsychological features of alcohol-related brain damage (ARBD) are well described, and the deficits appear to centre on visuospatial coordination, memory, abstract thinking and learning new information, with general knowledge, over-rehearsed

information and verbal skills largely spared (Lishman, 1998). Attempts have been made to describe the unique features of 'alcoholic dementia' (Oslin and Cary, 2003), but there is a lack of evidence linking any specific neuropathology with heavy alcohol intake (Joyce, 1994). A range of potential factors have been implicated in the causation of ARBD, including direct alcohol neurotoxicity, thiamine deficiency, traumatic brain injury, familial alcoholism, childhood psychopathology, age and education (Bates et al., 2002). Studies in people with features suggestive of WE have shown that their memory and general intellectual function are roughly equivalent (Bowden, 1990). Therefore, the effects of thiamine deficiency on cognition are more widespread than amnesia, with effects on visuospatial and abstracting functions being indicated (Jacobson et al., 1990).

The mechanism by which chronic heavy alcohol consumption causes thiamine deficiency is by increasing metabolic demand, decreasing dietary intake and reducing hepatic storage capacity due to liver damage (Cook et al., 1998, Thomson et al., 1987). Brain cells require three thiamine-dependent enzymes to metabolise glucose (transketolase, pyruvate dehydrogenase complex, and α-ketoglutarate dehydrogenase) (Butterworth, 1989), and a deficiency of thiamine reduces the activity of these enzymes leading to brain cell death and reduced cognitive function (Butterworth, 1989). Cognitive impairment due to subclinical WKS in alcohol dependence may therefore be responsive to thiamine therapy. Abstinence can also improve cognition and therefore it remains the mainstay of any effective prevention programme. This is important as apart from thiamine there are no established pharmacotherapeutic strategies to specifically prevent impairment of or improve cognition once a deficit has been established.

For those with established WKS appropriate rehabilitation, usually in supported accommodation for those with moderate and severe impairment is the correct approach as there is some evidence to suggest that people with WKS are capable of new learning, particularly if they live in a calm and well-structured environment and if new information is cued (Kopelman et al, 2009). There have been a few case reports of using medications to treat dementia in WKS with mixed results (Luykx et al, 2008; Cochrane et al, 2005). In an open study, the noradrenergic antidepressant, reboxetine did appear to improve cognitive performance in those who had WKS for less than a year (Reuster et al, 2003). Fluvoxamine has been shown to improve memory consolidation and/or retrieval in patients with WKS (Martin et al, 1995).

The NICE (2010b) guideline on the management of alcohol-related physical complications made recommendations about patients who did not have clinical features of WE, but were at high risk of developing it. They identified a high risk group who may be characterised by the following features:

- alcohol-related liver disease
- medically-assisted withdrawal from alcohol (planned or unplanned)
- acute alcohol withdrawal
- malnourishment or risk of malnourishment; this may include;
    - weight loss in past year
    - reduced BMI
    - loss of appetite
    - nausea and vomiting
    - a general impression of malnourishment
- homelessness

- hospitalised for acute illness
- hospitalised for comorbidity or another alcohol issue.

From the perspective of acute inpatient care the RCP guideline also recommended the use of intramuscular thiamine the group had concerns about the absorption of oral thiamine in a group undergoing assisted withdrawal. per 5 million pairs of Pabrinex ampoules, which is far lower than many frequently used drugs that carry no special warning in the BNF (Thomson and Cook, 1997, Thomson and Marshall, 2006).

Relatively little is also known about the outcomes of treatment of alcoholic Korsakoff syndrome. The large case study by Victor et al (1971) reported that 25% recovered, 50% showed improvement over time and 25% remained largely unchanged. Other authors also believe that some improvement does occur in approximately 75% of patients over a number of years is they remain abstinent from alcohol (Kopelman et al., 2009). There is little evidence from research studies to design and inform effective rehabilitation specifically in WKS (Smith & Hillman, 1999) although strategies developed in cognitive rehabilitation for a range of cognitive impairments may be of value (Cicerone *et al,* 2005).

7.11.1 Evidence into recommendations

The GDG accepted the evidence that thiamine as a key preventative role in WKS and adapted the recommendations developed by the RCP group and developed the recommendation to take account of thiamine's use in a community based populations. The principle that due to the high risk of long term brain injury and the potentially serious consequences of WE, that a low index of suspicion for WE be adopted and thiamine prescribed accordingly. A number of at risk groups are specified in the recommendation. The GDG also considered the care of people with established WKs and subsequent cognitive impairment. The limited data available suggested that continued abstinence from alcohol and a supportive and structured environment may have some beneficial effects for people with WKS and given the high morbidity and mortality in this group the GDG thought that that supported residential placement or for the those with mild impairment and 24 hour care for those with severe impairments should be made available.

7.11.2 Recommendations

7.11.2.1 Consider using thiamine to prevent Wernicke-Korsakoff syndrome (see NICE clinical guideline 100) in service users who:

- are undergoing assisted withdrawal
- have alcohol-related liver disease
- are malnourished or at risk of malnourishment
- are homeless.

7.11.2.2 For people with Wernicke-Korsakoff syndrome, offer long-term placement in:

- supported independent living for those with mild cognitive impairment
- supported 24-hour care for those with moderate or severe cognitive impairment

In both settings the environment should be adapted for people with cognitive

impairment and support provided to help service users maintain abstinence from alcohol.

8. Appendices

- 18a- Organisation of care GRADE tables
- 18b- Rehabilitation GRADE tables
- 18c- Psychological interventions GRADE tables
- 18d- Pharmacological interventions GRADE tables
- 18e- Health Economic evidence profiles

Appendix 19: Evidence tables for economic studies **On CD**

Appendix 1: Scope for the development of the clinical guideline

Final version

Date

1 Guideline title

Alcohol dependence and harmful use: diagnosis, assessment and management of harmful drinking and alcohol dependence

1.1 Short title

Alcohol dependence and harmful alcohol use

2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Mental Health to develop a clinical guideline on alcohol dependence and harmful alcohol use for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) NICE clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by NICE after an NSF has been issued have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, if appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) There are two main sets of diagnostic criteria in current use, the International Classification of Mental and Behavioural Disorders 10th Revision (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV). The ICD-10 definition of alcohol dependence (alcohol dependence syndrome) makes reference to a cluster of physiological, behavioural, and cognitive phenomena in which the use of alcohol takes a much higher priority than other behaviours. The DSM-IV defines a person with alcohol dependence as someone who continues the use of alcohol despite significant alcohol-related

problems. In terms of harmful alcohol use, the ICD-10 defines 'harmful use' as a pattern of drinking that causes damage to physical and mental health.

b) Psychiatric disorders and problems associated with alcohol dependence and harmful alcohol use include: depression, anxiety, personality disorders, post traumatic stress disorder, drug misuse, self-harm, suicide and brain damage. Alcohol use disorders are also associated with a wide range of physical problems, including liver disease, various cancers, heart disease and stroke.

c) The Alcohol Needs Assessment Research Project estimated that 38% of men and 16% of women aged between 16 and 64 have an alcohol use disorder, and that 6% of men and 2% of women have alcohol dependence. There is a lack of reliable UK data on prevalence rates of alcohol use disorders in children.

4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This scope defines what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on a referral from the Department of Health (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Young people (10 years and older) and adults with a diagnosis of alcohol dependence or harmful alcohol use.

4.1.2 Groups that will not be covered

a) Children younger than 10 years.

b) Pregnant women.

4.2 Healthcare setting

a) Care provided by primary, community and secondary healthcare and social care professionals who have direct contact with, and make decisions concerning, the

care of young people and adults with alcohol dependence or harmful alcohol use. This will include:

- care in general practice
- community- and residential-based care, including inpatient treatment and rehabilitation
- the primary/secondary care interface
- transition through the range of healthcare services from childhood to older adulthood
- the criminal justice system, including prison healthcare.

b) This is a guideline for alcohol services funded by or provided for the NHS. It will make recommendations for services provided within the NHS, social services, the independent sector and non-statutory services.

4.3 Clinical management

4.3.1 Areas that will be covered by the guideline

a) Definitions of alcohol dependence and harmful alcohol use according to the main diagnostic classification systems (ICD-10 and DSM-IV).

b) Early identification of alcohol dependence or harmful alcohol use in people in at-risk populations, in particular treatment-seeking populations, and identification of factors that should lead to investigation into the possibility of alcohol dependence or harmful alcohol use (please refer also to the prevention and clinical management guidance currently under development, see section 5).

c) Identifying people with alcohol dependence and harmful alcohol use in clinical practice, including the sensitivity and specificity of different methods, and thresholds.

d) Assessment, including identification and management of risk, and assessment of severity of alcohol-related problems, dependence and alcohol withdrawal.

e) Development of appropriate care pathways that support the integration of other NICE guidance on the management, treatment and aftercare of alcohol misuse.

f) The range of care routinely available in the NHS.

g) Pharmacological interventions, for example, initiation and duration of treatment, management of side effects and discontinuation. Specific pharmacological treatments considered will include:

- opioid antagonists (naltrexone and nalmefene)
- acamprosate
- disulfiram
- topiramate
- baclofen

- chlordiazepoxide
- serotogenic agents (selective serotonin reuptake inhibitors and serotonin-3 receptor antagonist, ondansetron).

h) Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

i) Common psychological and psychosocial interventions currently provided, for example, 12-step programmes, cognitive behavioural therapy, motivational enhancement therapy, relapse prevention, contingency management and community reinforcement approach.

j) Low intensity psychological interventions, for example, referral to Alcoholics Anonymous and guided self-help.

k) Combined pharmacological and psychological/psychosocial treatments.

l) Management of alcohol withdrawal in community and residential settings.

m) Management of common mental health problems and drug misuse in the context of alcohol dependence, if this differs from their management alone.

n) Prevention and management of neuropsychiatric complications of alcohol dependence or harmful alcohol use including:

- alcohol related brain damage
- Wernicke–Korsakoff syndrome.

o) Sensitivity to different beliefs and attitudes of people of different genders, races and cultures, and issues of social exclusion.

p) The role of family and carers in the treatment and support of people with alcohol dependence and harmful alcohol use (with consideration of choice, consent and help), and support that may be needed by family and carers (such as conjoint marital therapy and family therapy).

q) The Guideline Development Group will consider making recommendations on complementary interventions or approaches to care relevant to alcohol dependence and harmful alcohol use.

r) The Guideline Development Group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources, can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

4.3.2 *Areas that will not be covered by the guideline*

a) Treatments not normally made available by the NHS.

b) The separate management of comorbid conditions.

c) The management of acute alcohol withdrawal in the emergency department and general medical and surgical settings. This will be covered in 'Alcohol-use disorders in adults and young people: clinical management' (publication expected May 2010).

d) The prevention and management of Wernicke's encephalopathy. This will be covered in 'Alcohol-use disorders in adults and young people: clinical management' (publication expected May 2010).

4.4 Status

4.4.1 Scope

a) This is final scope.

b)

4.4.2 Guideline

a) The development of the guideline recommendations will begin in March 2009.

b)

5 Further information

a) The guideline development process is described in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

b) These are available from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

Appendix 2: Declarations of interests by GDG members

Declarations of interest	
Professor Colin Drummond - Chair, Guideline Development Group	
Employment	Professor of Addiction Psychiatry, Institute of Psychiatry, Kings College London
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	In receipt of research grants on alcohol research from the Medical Research Council, the European Commission, the Department of Health, the Home Office, the Scottish Government, and the World Health Organisation. (declared December 2008) A member of the World Health Organisation Expert Committee on Alcohol Problems and receive travel and subsistence while working for WHO. (declared December 2008) I have received an educational grant from Alkermes Inc (manufacturers of Vivitrol) to the value of £5,000 in 2008 which is held at the Institute of Psychiatry. (declared December 2008)
Personal non-pecuniary interest	None
Mr Adrian Brown	
Employment	Alcohol Nurse Specialist, St Mary's Hospital, Imperial College
Personal pecuniary interest	Consultancy- attending focus groups of professionals and acting as 'expert' on site at conference presentation.Archimedes Pharma- educational material for Wernike-Korsakoff and Pabrinex. Received £250 + £550 and travel for two events. (declared July 2009)
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Professor Alex Copello	
Employment	Professor of Addiction Research, University of Birmingham
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Professor Anne Lingford-Hughes	

Employment	Professor of Addiction Biology, Imperial College London and Central North West London NHS Foundation Trust.
Personal pecuniary interest	Bristol Myers Squibb, member of Core Faculty; current though no monies in last 12 months. Janssen-Cilag; Paid speaker: educational event, my talk on dual disorder was not about promoting one of their products. (declared January 2009) CINP psychopharmacology certificate – two lectures on psychopharmacology of alcohol abuse: sponsored by Servier (declared January 2010) Meeting organised by pharmacology special interest group- presentation on comorbidity and managing substance misuse (declared March 2010) Talk at meeting organised by Eli Lilly on bipolar disorder and alcoholism (declared March 2010)
Personal family interest	None
Non-personal pecuniary interest	NIHR grant to study pharmacology in alcohol detox. (declared July 09)
Personal non-pecuniary interest	Co-ordinated British Association for Psychopharmacology guidelines which covered treatment of alcohol dependence. Published 2004. (declared January 2009) Leading revision of BAP guidelines in substance misuse and addiction (declared November 09) putting in a grant for an RCT involving baclofen (declared November 09) Coordinating update of BAP guidelines in addiction (declared January 2010) Shortlisted for HTA grant for RCT of baclofen in alcohol dpeendence (declared January 2010)
Mr Brendan Georgeson	
Employment	Treatment Coordinator, Walsingham House, Bristol
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Individual member of The Federation of Drug and Alcohol Professionals. (declared January

	2009) Member of the Society for the Study of Addiction. (declared January 2009) Associate Member of the Institute of Healthcare Management (declared January 2009) Trustee of Posative Images, a charity that uses film production to produce mentoring/ training resources (declared April 2010)
Dr Edward Day	
Employment	Senior Lecturer and Consultant in Addiction Psychiatry, University of Birmingham
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	I am a principal investigator on two grants in the substance misuse field (ACTAS study and COMBAT studies). I have published papers on alcohol detoxification, management of Wernickes-Korsakiff syndrome and liver transplantation for alcoholic liver disease. (declared March 2009)
Dr Eilish Gilvarry	
Employment	Consultant Director in Addictions, and Assistant Medical Director, Northumberland, Tyne & Wear NHS Trust
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Ms Jan Fry	
Employment	Carer Representative and voluntary sector consultant
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Ms Jayne Gosnall	
Employment	Service User Representative and Treasurer of Salford Drug and Alcohol Forum
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Mr John Dervan	

Employment	Lay member and Retired Alcohol Treatment Agency CEO
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Trustee, CASA Alcohol Services (declared January 2009)
Dr Julia Sinclair	
Employment	Senior Lecturer in Psychiatry, University of Southampton
Personal pecuniary interest	
Personal family interest	My husband, a psychopharmacologist has consulted for a number of companies who make treatments for anxiety or depression. His work does not include any treatments for alcohol use disorders. (declared Jan 2009)
Non-personal pecuniary interest	Part of research project funded by MRC piloting Assertive Community Treatment in alcohol dependence. (declared March 2009)
Personal non-pecuniary interest	Gave a talk on non-promotional training course run by the 'Lundbeck Institute' on complex depression. Talk was on suicide and comorbidity (including alcohol). (declared June 2009)
Dr Linda Harris	
Employment	Clinical Director Wakefield Integrated Substance Misuse Service and Director of the RCGP Substance Misuse Unit
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	In receipt of an educational grant from Schering Plough to support clinical leadership development support across the health and social care stakeholder groups working in the Wakefield Integrated Substance Misuse Service. This is being delivered in the full knowledge of the local PCT and is being conducted within ABPI guidance. (declared January 2009) A grant has been deployed to fund an independent management consultancy firm called Healthskills Consulting Ltd, who have supported leadership development and O & D of the drug misuse treatment system. ABPI rules obeyed and PCT aware. (declared March 2009) Over the years RCGP SMU has been in receipt of educational grants to support specials

	substance misuse workforce development and training standards (declared March 2009).
Personal non-pecuniary interest	None
Dr Marsha Morgan	
Employment	Reader in Medicine and Honorary Consultant Physician, University of London Medical School
Personal pecuniary interest	I am a member of the Advisory board of the Institute of Alcohol Studies. I receive an annual stipend of £1,500 which I contribute to my University Research Account. (declared January 2009) I have taken part in symposia both in the UK and abroad on the Pharmacotherapy of Alcohol Dependence. On some occasions my travel and subsistence have been covered by one of the Pharmaceutical companies but I have not accepted lecture fees. (declared January 2009)
Personal family interest	None
Non-personal pecuniary interest	Between eight and 10 years ago I undertook pharmacotherapeutic trials in alcohol dependent patients for Du Pont Pharmaceuticals and Lipha Pharmaceuticals. Per capita fees were paid for recruited patients to the Royal Free Hospital Medical School for whom I worked. (declared January 2009)
Personal non-pecuniary interest	None
Dr Pamela Roberts	
Employment	Consultant Clinical and Forensic Psychologist, Cardiff Addictions Unit
Personal pecuniary interest	Small grant received from AERC with regard to small scale project studying the relationship between Pabrinex and cognitive functioning. (declared March 2010).
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Welsh Representative for the BPS Faculty of Addiction (declared April 2010).
Mrs Stephenie Noble	
Employment	Registered Manager/Nursing Manager, Broadway Lodge
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Mr Tom Phillips	
Employment	Consultant Nurse, Addiction Humber NHS

	Foundation Trust
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	PI on two projects, as stated in application for post. Both explore screening and brief interventions. SIPS trial and AESOPS. SIPS trial DH funded and AESOPS trial HTA funded. (declared April 2009) NIHR- Clincal Doctoral Research Fellowship in area of alcohol research from Jan 2010-2015. (declared October 2009)
Mr Trevor McCarthy	
Employment	Independent Consultant
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Since September 2008 my employment has been as a self-employed consultant specialising particularly in work in the alcohol field. In this capacity I have worked with a voluntary sector provider; for a Drug & Alcohol Action Team and for Alcohol Concern, delivering services to PCTs and to the Regional Office on behalf of the Department of Health. (declared January 2009) My previous role included managing the production of the *Review of effectiveness of treatment for alcohol problems* which includes the research evidence relevant to this guideline. I was also involved in the development of *Models of Care for Alcohol Misusers*. (declared January 2009) I have also given presentations at conferences and other events which have included comment on the issues under consideration. The bulk of my employment experience has been gained in the non-statutory sector managing the delivery of community alcohol and drug treatment services. (declared January 2009) It could be that some might interpret such activities as my having compromised my views and objectivity. My own view is that this experience qualifies me to make an application to the Institute and I do not believe that my past work could reasonably have been construed as

	contentious or biased. (declared January 2009)
National Collaborating Centre for Mental Health Staff	
Dr Amina Udechuku	
Employment	Systematic Reviewer, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Ms Esther Flanagan	
Employment	Guideline Development Manager, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Dr Ifigeneia Mavranezouli	
Employment	Senior Health Economist, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Ms Laura Shields	
Employment	Research assistant, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Mr Matt Dyer	
Employment	Health Economist, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Mr Rob Saunders	
Employment	Research Assistant, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Ms Sarah Stockton	

Employment	Senior Information Scientist, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Professor Steve Pilling	
Employment	Joint Director, National Collaborating Centre for Mental Health; Director, Centre for Outcomes Research and Effectiveness, University College London.
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Dr Suffiya Omarjee	
Employment	Health Economist, National Collaborating Centre for Mental Health
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None

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Appendix 3: Special advisors to the Guideline Development Group

Dr John Lewis

Appendix 4: Stakeholders who responded to early requests for evidence

Appendix 5: Stakeholders and experts who submitted comments in response to the consultation draft of the guideline

Stakeholders
Experts

Appendix 6: Researchers contacted to request information about studies

Dr Bert Aertgeerts
Dr Lynn Alden
Dr Gerard Connors
Dr David Foy
Dr Peter Friedmann
Dr J. C. Garbutt
Dr Ronan Hearne
Dr Rachel Humeniuk
Dr Hakan Kallmen
Dr David Kavanagh
Dr Mark Litt
Professor Richard Longabaugh
Professor Karl Mann
Proffessor John Monterosso
Dr Kathryn Rost
Janice Vendetti (Project MATCH coordinating Centre)
Dr Kim Walitzer
Professor Paul Wallace

Appendix 7: Clinical questions

1. For people who misuse alcohol, what are their experiences of having problems with alcohol, of access to services and of treatment?

2. For families and carers of people who misuse alcohol, what are their experiences of caring for people with an alcohol problem and what support is available for families and carers?

3. In adults with alcohol misuse, what is the clinical efficacy, cost-effectiveness, and safety of, and patient satisfaction associated with different systems for the organisation of care?

4. What are the most effective a) diagnostic and b) assessment tools for alcohol dependence and harmful alcohol use?

5. What are the most effective ways of monitoring clinical progress in alcohol dependence and harmful alcohol use?

6. To answer questions 4 and 5, what are the advantages, disadvantages, and clinical utility of:
   - The structure of the overall clinical assessment
   - Biological measures
   - Psychological/behavioural measures
   - Neuropsychiatric measures (including cognitive impairment)
   - Physical assessment?

7. In adults in planned alcohol withdrawal, what is the clinical efficacy, cost effectiveness, safety of, and patient satisfaction associated with:
   - preparatory work before withdrawal
   - different drug regimens
   - the setting (that is, community , residential or inpatient)?

8. In adults in planned alcohol withdrawal what factors influence the choice of setting in terms of clinical and cost effectiveness including:
   - severity of the alcohol disorder
   - physical comorbidities
   - psychological comorbidities
   - social factors

9. In adults with harmful or dependent alcohol use what are the preferred structures for and components of community-based and residential specialist alcohol services to promote long-term clinical and cost-effective outcomes?

10. For people with alcohol dependence or harmful alcohol use is psychological *treatment x* when compared to *y* more clinically and cost-effective and does this depend on:

- Presence of comorbidities
- Subtypes (matching effects)

- Therapist-related factors (quality, therapeutic alliance, competence, training, etc.)

11. What are the most effective a) diagnostic and b) assessment tools for alcohol dependence and harmful alcohol use in children and young people (aged 10-18 years)?

12. What are the most effective ways of monitoring clinical progress in alcohol dependence and harmful alcohol use in children and young people (aged 10-18 years)?

13. For children and young people with alcohol dependence or harmful alcohol use is *treatment x* when compared to *y* more clinically and cost-effective and does this depend on the presence of comorbidities?

14. For people with alcohol dependence or harmful alcohol what pharmacological interventions are more clinically and cost-effective?

15. What are the impacts of severity and comorbities on outcomes?

16. When should pharmacological treatments be initiated and for what duration should they be prescribed?

1 Appendix 8: Review protocols

Relevant questions	EXAMPLE::2.1.1a For people with first-episode or early schizophrenia, what are the benefits and downsides of continuous antipsychotic drug[39] treatment when compared to alternative management strategies at the initiation of treatment[40]?
Sub-questions	**2.1.3, 2.14a, 2.1.5a, 2.2.1, 2.2.5, 2.2.6, 2.2.7**
Chapter	?
Sub-section	?
Topic Group	Pharm
Sub-section lead	?
Search strategy	**Databases:** CINAHL, EMBASE, MEDLINE, PSYCINFO, CENTRAL, CDSR, DARE **Additional sources:** Reference lists of included studies, systematic reviews published after 2002.
Existing reviews	
• **Updated**	
• **Not updated**	
Search filters used	SR and RCT (See Appendix 9)
Question specific search filter	N/A – generic searches conducted
Amendments to filter/ search strategy	None
Eligibility criteria	
• Intervention	Antipsychotic drugs licensed for use in the UK (BNF 54): First-generation: • Benperidol • Chlorpromazine hydrochloride • Flupentixol • Fluphenazine hydrochloride • Haloperidol • Levomepromazine • Pericyazine • Perphenazine • Pimozide • Prochlorperazine • Promazine hydrochloride • Sulpiride • Trifluoperazine

[39] The analysis will be conducted separately for each antipsychotic drug licensed for use in the UK.
[40] When administered within the recommended dose range (BNF 54).

	• Zuclopenthixol acetate • Zuclopenthixol dihydrochloride Second-generation: • Amisulpride • Aripiprazole • Clozapine • Olanzapine • Quetiapine • Risperidone • Sertindole • Zotepine Antipsychotic depot injections: • Flupentixol decanoate • Fluphenazine decanoate • Haloperidol • Pipotiazine palmitate • Risperidone • Zuclopenthixol decanoate
• Comparator	Any relevant alternative management strategy
• Population (including age, gender etc)	Adults (18+) with first-episode or early schizophrenia
• Outcomes (see Outcomes document for definitions)	-Mortality (suicide & natural causes) -Global state (including relapse) -Service outcomes -Mental state -Psychosocial functioning -Behaviour -Engagement with services -Cognitive functioning -QoL -Satisfaction with treatment/ subjective well-being -Adherence to medication/ study protocol -Adverse events (including extrapyramidal side effects, weight gain, sedation/fatigue, sexual dysfunction, diabetes/disturbance of glucose homeostasis, increased prolactin, cardiotoxicity, suicide, depression)
• Study design	RCT
• Publication status	[Published and unpublished (if criteria met)]
• Year of study	2002-2007
• Dosage	[Enter relevant information]
• Minimum	[Enter relevant information]

sample size	
• Study setting	[Enter relevant information]
Additional assessments	An additional assessment will be undertaken to ensure that restriction to experimental study designs does not result in overlooking the effects of X that are difficult to quantify and have not been captured in these studies. Studies were categorised as short-term (<12 weeks), medium-term (12–51 weeks) and long-term (52 weeks or more). Sensitivity analyses: • Exclude studies without blinded/masked assessment • Exclude studies that didn't use ITT • Exclude studies that used LOCF

1

2

Appendix 9: Search strategies for the identification of clinical studies

The search strategies should be referred to in conjunction with information set out in Section 3.2.9.

For standard mainstream bibliographic databases (AMED, CINAHL, EMBASE, MEDLINE and PsycINFO) search terms on alcohol dependence and harmful alcohol use were combined with study design filters for systematic reviews, randomised controlled trials and qualitative research. For searches generated in databases with collections of study designs at their focus (DARE, CDSR, CENTRAL and HTA) search terms on alcohol dependence and harmful alcohol use were used without a filter. The search strategies were initially developed for Medline before being translated for use in other databases/interfaces.

A condensed version of the strategies constructed for use with the main databases searched follows:

1. Guideline topic search strategy

a. MEDLINE, EMBASE, PsycINFO – Ovid SP interface

1. exp alcohol abuse/ or (alcohol-related disorders or alcohol-induced disorders or sobriety).sh.
2. (alcoholi$ or (alcohol$ and (abstinence or detoxification or intoxicat$ or rehabilit$ or withdraw$))).hw.
3. *abuse/ or *addiction/ or *drug abuse/ or *substance related disorders/
4. alcoholi$.ti,ab.
5. (drinker$1 or (drink$ adj2 use$1) or ((alcohol$ or drink$) adj5 (abstinen$ or abstain$ or abus$ or addict$ or attenuat$ or binge$ or crav$ or dependen$ or detox$ or disease$ or disorder$ or excessiv$ or harm$ or hazard$ or heavy or high risk or intoxicat$ or misus$ or overdos$ or (over adj dos$) or problem$ or rehab$ or reliance or reliant or relaps$ or withdraw$))).ti,ab.
6. (control$ adj2 drink$).tw.
7. sobriet$.ti,ab,hw.
8. or/1-7

** Search request #3 was used to search for evidence of systematic reviews only.*

b. CINAHL – Ebsco interface

S11 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10
S10 TI sobriet* or AB sobriet*
S9 (TI control* N2 drink*) or (AB control* N2 drink*)
S8 (TI drink* N5 abstinen* or AB drink* N5 abstinen*) or (TI drink* N5 abstain* or AB drink* N5 abstain*) or (TI drink* N5 abus* or AB drink* N5 abus*) or (TI drink* N5 addict* or AB drink* N5 addict*) or (TI drink* N5 attenuat* or AB drink* N5 attenuat*) or (TI drink* N5 binge* or AB drink* N5 binge*) or (TI drink* N5 crav* or AB drink* N5 crav*) or (TI

		drink* N5 dependen* or AB drink* N5 dependen*) or (TI drink* N5 detox* or AB drink* N5 detox*) or (TI drink* N5 disease* or AB drink* N5 disease*) or (TI drink* N5 disorder* or AB drink* N5 disorder*) or (TI drink* N5 excessiv* or AB drink* N5 excessiv*) or (TI drink* N5 harm* or AB drink* N5 harm*) or (TI drink* N5 hazard* or AB drink* N5 hazard*) or (TI drink* N5 heavy or AB drink* N5 heavy) or (TI drink* N5 high risk or AB drink* N5 high risk) or (TI drink* N5 intoxicat* or AB drink* N5 intoxicat*) or (TI drink* N5 misus* or AB drink* N5 misus*) or (TI drink* N5 overdos* or AB drink* N5 overdos*) or (TI drink* N5 over dos* or AB drink* N5 over dos*) or (TI drink* N5 problem* or AB drink* N5 problem*) or (TI drink* N5 rehab* or AB drink* N5 rehab*) or (TI drink* N5 reliance or AB drink* N5 reliance) or (TI drink* N5 reliant or AB drink* N5 reliant) or (TI drink* N5 relaps* or AB drink* N5 relaps*) or (TI drink* N5 withdraw* or AB drink* N5 withdraw*)
	S7	(TI alcohol* N5 abstinen* or AB alcohol* N5 abstinen*) or (TI alcohol* N5 abstain* or AB alcohol* N5 abstain*) or (TI alcohol* N5 abus* or AB alcohol* N5 abus*) or (TI alcohol* N5 addict* or AB alcohol* N5 addict*) or (TI alcohol* N5 attenuat* or AB alcohol* N5 attenuat*) or (TI alcohol* N5 binge* or AB alcohol* N5 binge*) or (TI alcohol* N5 crav* or AB alcohol* N5 crav*) or (TI alcohol* N5 dependen* or AB alcohol* N5 dependen*) or (TI alcohol* N5 detox* or AB alcohol* N5 detox*) or (TI alcohol* N5 disease* or AB alcohol* N5 disease*) or (TI alcohol* N5 disorder* or AB alcohol* N5 disorder*) or (TI alcohol* N5 excessiv* or AB alcohol* N5 excessiv*) or (TI alcohol* N5 harm* or AB alcohol* N5 harm*) or (TI alcohol* N5 hazard* or AB alcohol* N5 hazard*) or (TI alcohol* N5 heavy or AB alcohol* N5 heavy) or (TI alcohol* N5 high risk or AB alcohol* N5 high risk) or (TI alcohol* N5 intoxicat* or AB alcohol* N5 intoxicat*) or (TI alcohol* N5 misus* or AB alcohol* N5 misus*) or (TI alcohol* N5 overdos* or AB alcohol* N5 overdos*) or (TI alcohol* N5 over dos* or AB alcohol* N5 over dos*) or (TI alcohol* N5 problem* or AB alcohol* N5 problem*) or (TI alcohol* N5 rehab* or AB alcohol* N5 rehab*) or (TI alcohol* N5 reliance or AB alcohol* N5 reliance) or (TI alcohol* N5 reliant or AB alcohol* N5 reliant) or (TI alcohol* N5 relaps* or AB alcohol* N5 relaps*) or (TI alcohol* N5 withdraw* or AB alcohol* N5 withdraw*)
	S6	(TI drink* N2 use*) or (AB drink* N2 use*)
	S5	TI drinker* or AB drinker*
	S4	(MM "Substance Use Disorders") or (MM "Behavior, Addictive") or (MM "Substance Abuse")
	S3	MW alcoholi*
	S2	MW alcohol* and (abstinence or detoxification or intoxicat* or rehabilit* or withdraw*)
	S1	(MH "Alcohol Abuse") or (MH "Alcoholic Intoxication") or (MH "Alcoholism") or (MH "Alcohol-Related Disorders") or (MH "Alcohol Abuse Control (Saba CCC)") or (MH "Alcohol Abuse (Saba CCC)")

** Search request #4 was used to search for evidence of systematic reviews only.*

c. Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials – Wiley Interscience interface

#1	MeSH descriptor Alcohol-Related Disorders, this term only
#2	MeSH descriptor Alcohol-Induced Disorders, this term only
#3	MeSH descriptor Alcoholic Intoxication, this term only
#4	MeSH descriptor Alcoholism, this term only
#5	(alcoholi*):ti or (alcoholi*):ab
#6	(abstinence or detoxification or intoxicat* or rehabilit* or withdraw*):kw and (alcohol*):kw
#7	MeSH descriptor Substance-Related Disorders, this term only
#8	(drinker* or (drink* NEAR/2 use*) or ((alcohol* or drink*) NEAR/5 (abstinen* or abstain* or abus* or addict* or attenuat* or binge* or crav* or dependen* or detox* or disease* or disorder* or excessiv* or harm* or hazard* or heavy or high risk or intoxicat* or misus* or overdos* or over dose or over dosing or over doses or problem* or rehab* or reliance or reliant or relaps* or withdraw*))):ti or (drinker* or (drink* NEAR/2 use*) or ((alcohol* or drink*) NEAR/5 (abstinen* or abstain* or abus* or addict* or attenuat* or binge* or crav* or dependen* or detox* or disease* or disorder* or excessiv* or harm* or hazard* or heavy or high risk or intoxicat* or misus* or overdos* or over dose or over dosing or over doses or problem* or rehab* or reliance or reliant or relaps* or withdraw*))):ab
#9	(control* NEAR/2 drink*):ti or (control* NEAR/2 drink*):ab
#10	(sobriet*):ti or (sobriet*):ab
#11	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)

2. Systematic review search filter – this is an adaptation of a filter designed by the Health Information Research Unit of the McMaster University, Ontario.

a. MEDLINE, EMBASE, PsycINFO – Ovid SP interface

1	(literature review or systematic review$ or meta anal$).sh,id. or "review literature as topic"/
2	((analy$ or evidence$ or methodol$ or quantativ$ or systematic$) adj5 (overview$ or review$)).tw. or ((analy$ or assessment$ or evidence$ or methodol$ or quantativ$ or qualitativ$ or systematic$).ti. and review$.ti,pt.) or (systematic$ adj5 search$).ti,ab.
3	((electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh. or (bids or cochrane or embase or index medicus or isi citation or medline or psyclit or psychlit or scisearch or science citation or (web adj2 science)).tw. or cochrane$.sh.) and (review$.ti,ab,sh,pt. or systematic$.ti,ab.)
4	(metaanal$ or meta anal$ or metasynthes$ or meta synethes$).ti,ab.
5	(research adj (review$ or integration)).ti,ab.
6	reference list$.ab.
7	bibliograph$.ab.
8	published studies.ab.
9	relevant journals.ab.
10	selection criteria.ab.
11	(data adj (extraction or synthesis)).ab.
12	(handsearch$ or ((hand or manual) adj search$)).ti,ab.
13	(mantel haenszel or peto or dersimonian or der simonian).ti,ab.

14 (fixed effect$ or random effect$).ti,ab.
15 meta$.pt. or (literature review or meta analysis or systematic review).md.
16 ((pool$ or combined or combining) adj2 (data or trials or studies or results)).ti,ab.
17 or/1-16

b. CINAHL – Ebsco interface

S32 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S22 or S23 or S26 or S27 or S28 or S29 or S30 or S31
S31 TI (analy* N5 review* or evidence* N5 review* or methodol* N5 review* or quantativ* N5 review* or systematic* N5 review*) or AB (analy* N5 review* or assessment* N5 review* or evidence* N5 review* or methodol* N5 review* or qualitativ* N5 review* or quantativ* N5 review* or systematic* N5 review*)
S30 TI (pool* N2 results or combined N2 results or combining N2 results) or AB (pool* N2 results or combined N2 results or combining N2 results)
S29 TI (pool* N2 studies or combined N2 studies or combining N2 studies) or AB (pool* N2 studies or combined N2 studies or combining N2 studies)
S28 TI (pool* N2 trials or combined N2 trials or combining N2 trials) or AB (pool* N2 trials or combined N2 trials or combining N2 trials)
S27 TI (pool* N2 data or combined N2 data or combining N2 data) or AB (pool* N2 data or combined N2 data or combining N2 data)
S26 S24 and S25
S25 TI review* or PT review*
S24 TI analy* or assessment* or evidence* or methodol* or quantativ* or qualitativ* or systematic*
S23 TI “systematic* N5 search*” or AB “systematic* N5 search*”
S22 (S17 or S18 or S19) and (S20 or S21)
S21 TI systematic* or AB systematic*
S20 TX review* or MW review* or PT review*
S19 (MH "Cochrane Library")
S18 TI (bids or cochrane or embase or “index medicus” or “isi citation” or medline or psyclit or psychlit or scisearch or “science citation” or web N2 science) or AB (bids or cochrane or “index medicus” or “isi citation” or psyclit or psychlit or scisearch or “science citation” or web N2 science)
S17 TI (“electronic database*” or “bibliographic database*” or “computeri?ed database*” or “online database*”) or AB (“electronic database*” or “bibliographic database*” or “computeri?ed database*” or “online database*”)
S16 (MH "Literature Review")
S15 PT systematic* or PT meta*
S14 TI (“fixed effect*” or “random effect*”) or AB (“fixed effect*” or “random effect*”)
S13 TI (“mantel haenszel” or peto or dersimonian or “der simonian”) or AB (“mantel haenszel” or peto or dersimonian or “der simonian”)
S12 TI (handsearch* or "hand search*" or "manual search*") or AB (handsearch* or "hand search*" or "manual search*")
S11 AB "data extraction" or "data synthesis"
S10 AB "selection criteria"

S9 AB "relevant journals"
S8 AB "published studies"
S7 AB bibliograph*
S6 AB "reference list*"
S5 TI ("research review*" or "research integration") or AB ("research review*" or "research integration")
S4 TI (metaanal* or "meta anal*" or metasynthes* or "meta synethes*") or AB (metaanal* or "meta anal*" or metasynthes* or "meta synethes*")
S3 (MH "Meta Analysis")
S2 (MH "Systematic Review")
S1 (MH "Literature Searching+")

3. Randomised controlled trial search filter – this is an adaptation of a filter designed by the Health Information Research Unit of the McMaster University, Ontario.

a. MEDLINE, EMBASE, PsycINFO – Ovid SP interface

1 exp clinical trials/ or (crossover procedure or double blind procedure or placebo$ or randomization or random sample or single blind procedure).sh.
2 exp clinical trial/ or cross-over studies/ or double-blind method/ or random allocation/ or randomized controlled trials as topic/ or single-blind method/
3 exp clinical trials/ or (placebo or random sampling).sh,id.
4 (clinical adj2 trial$).tw.
5 (crossover or cross over).tw.
6 (((single$ or doubl$ or trebl$ or tripl$) adj5 blind$) or mask$ or dummy or singleblind$ or doubleblind$ or trebleblind$ or tripleblind$).tw.
7 (placebo$ or random$).mp.
8 (clinical trial$ or controlled clinical trial$ or random$).pt. or treatment outcome$.md.
9 animals/ not human$.mp.
10 animal$/ not human$/
11 (animal not human).po.
12 (or/1-8) not (or/9-11)

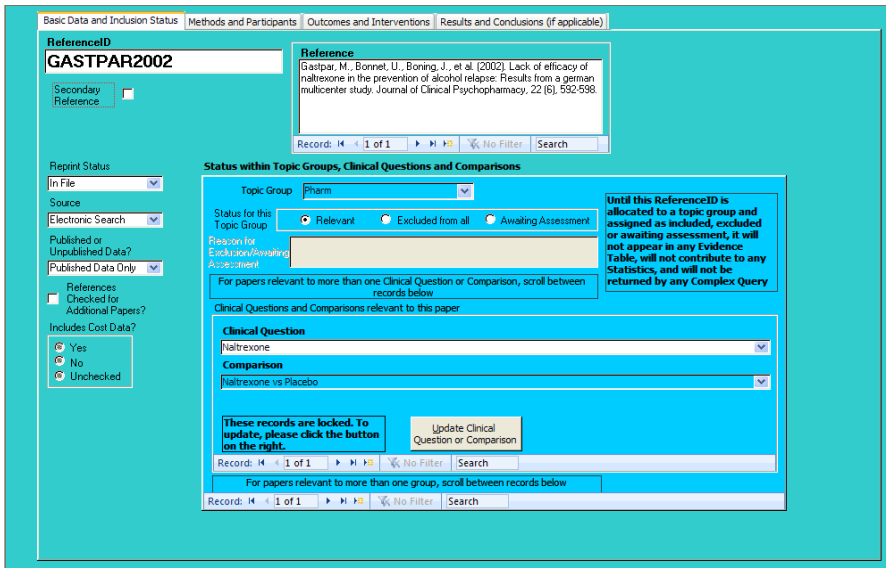
b. CINAHL – Ebsco interface

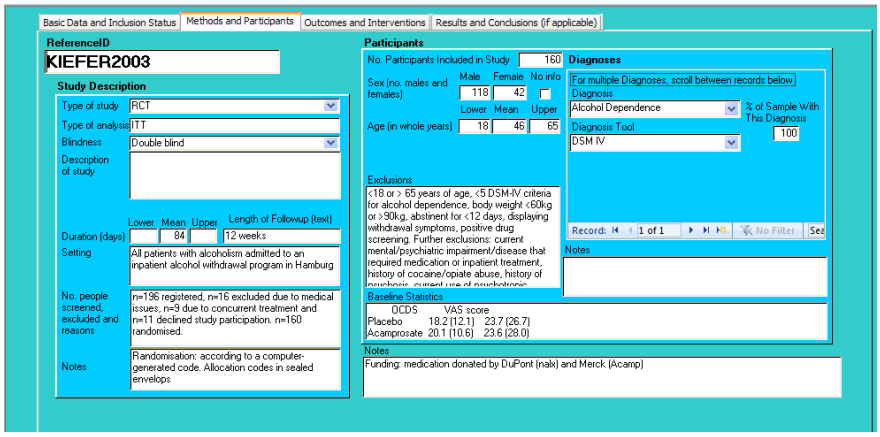
S11 S9 not S10
S10 (MH "Animals") not (MH "Human")
S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S8 (PT "Clinical Trial")
S7 TI (placebo* or random*) or AB (placebo* or random*)
S6 TI (single blind* or double blind* or treble blind* or mask* or dummy* or singleblind* or doubleblind* or trebleblind* or tripleblind*) or AB (single blind* or double blind* or treble blind* or mask* or dummy* or singleblind* or doubleblind* or trebleblind* or tripleblind*)
S5 TI (crossover or cross over) or AB (crossover or cross over)
S4 TI clinical N2 trial* or AB clinical N2 trial*

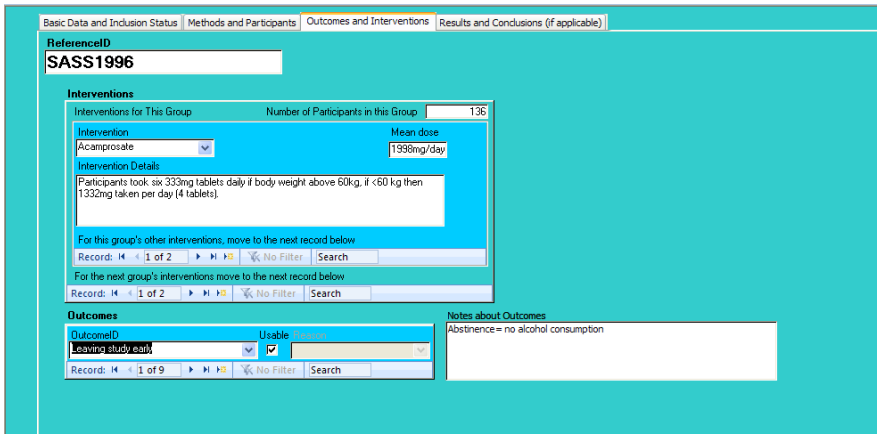
S3	(MH "Crossover Design") or (MH "Placebos") or (MH "Random Assignment") or (MH "Random Sample")
S2	MW double blind* or single blind* or triple blind*
S1	(MH "Clinical Trials+")

Details of additional searches undertaken to support the development of this guideline (qualitative, and AMED) are available on CD/on request.

Appendix 10: Clinical study data extraction form







Appendix 11: Quality checklists for clinical studies and reviews

The methodological quality of each study was evaluated using dimensions adapted from SIGN (SIGN, 2001). SIGN originally adapted its quality criteria from checklists developed in Australia (Liddel et al., 1996). Both groups reportedly undertook extensive development and validation procedures when creating their quality criteria.

Quality Checklist for a Systematic Review or Meta-Analysis			
Study ID:			
Guideline topic:		Key question no:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well-conducted systematic review:		In this study this criterion is: *(Circle one option for each question)*	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	A description of the methodology used is included.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The literature search is sufficiently rigorous to identify all the relevant studies.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	Study quality is assessed and taken into account.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	There are enough similarities between the studies selected to make combining them reasonable.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise bias? *Code* ++, + *or* –		

Notes on the use of the methodology checklist: systematic reviews and meta-analyses

Section 1 identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review — that is, making sure that it has been carried out carefully and that the outcomes are likely to be attributable to the intervention being investigated. Each question covers an aspect of methodology that research has shown makes a significant difference to the conclusions of a study.

For each question in this section, one of the following should be used to indicate how well it has been addressed in the review:

- well covered
- adequately addressed
- poorly addressed
- not addressed (that is, not mentioned or indicates that this aspect of study design was ignored)
- not reported (that is, mentioned but insufficient detail to allow assessment to be made)
- not applicable.

1.1 The study addresses an appropriate and clearly focused question

Unless a clear and well-defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question to be answered on the basis of the conclusions.

1.2 A description of the methodology used is included

One of the key distinctions between a systematic review and a general review is the systematic methodology used. A systematic review should include a detailed description of the methods used to identify and evaluate individual studies. If this description is not present, it is not possible to make a thorough evaluation of the quality of the review, and it should be rejected as a source of level-1 evidence (though it may be useable as level-4 evidence, if no better evidence can be found).

1.3 The literature search is sufficiently rigorous to identify all the relevant studies

A systematic review based on a limited literature search — for example, one limited to MEDLINE only — is likely to be heavily biased. A well-conducted review should as a minimum look at EMBASE and MEDLINE and, from the late 1990s onward, the Cochrane Library. Any indication that hand searching of key journals, or follow-up of reference lists of included studies, were carried out in addition to electronic database searches can normally be taken as evidence of a well-conducted review.

1.4 Study quality is assessed and taken into account

A well-conducted systematic review should have used clear criteria to assess whether individual studies had been well conducted before deciding whether to include or exclude them. If there is no indication of such an assessment, the review should be rejected as a source of level-1 evidence. If details of the assessment are poor, or the methods are considered to be inadequate, the quality of the review should be downgraded. In either case, it may be worthwhile obtaining and evaluating the individual studies as part of the review being conducted for this guideline.

1.5 There are enough similarities between the studies selected to make combining them reasonable

Studies covered by a systematic review should be selected using clear inclusion criteria (see question 1.4 above). These criteria should include, either implicitly or explicitly, the question of whether the selected studies can legitimately be compared. It should be clearly ascertained, for example, that the populations covered by the studies are comparable, that the methods used in the investigations are the same, that the outcome measures are comparable and the variability in effect sizes between studies is not greater than would be expected by chance alone.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on the responses in Section 1 and using the following coding system:

++	All or most of the criteria have been fulfilled. Where they have not been fulfilled, the conclusions of the study or review are thought **very unlikely** to alter.
+	Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.
–	Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

Quality Checklist for an RCT			
Study ID:			
Guideline topic:		**Key question no:**	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well-conducted RCT study:		**In this study this criterion is: (Circle one option for each question)**	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	The assignment of subjects to treatment groups is randomised.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	An adequate concealment method is used.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	Subjects and investigators are kept 'blind' about treatment allocation.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The treatment and control groups are similar at the start of the trial.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

1.6	The only difference between groups is the treatment under investigation.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?		
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise bias? *Code* ++, + *or* –		

Notes on the use of the methodology checklist: RCTs

Section 1 identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review — that is, making sure that it has been carried out carefully and that the outcomes are likely to be attributable to the intervention being investigated. Each question covers an aspect of methodology that research has shown makes a significant difference to the conclusions of a study.

For each question in this section, one of the following should be used to indicate how well it has been addressed in the review:

- well covered
- adequately addressed
- poorly addressed
- not addressed (that is, not mentioned or indicates that this aspect of study design was ignored)
- not reported (that is, mentioned but insufficient detail to allow assessment to be made)
- not applicable.

1.1 The study addresses an appropriate and clearly focused question

Unless a clear and well-defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question to be answered on the basis of its conclusions.

1.2 The assignment of subjects to treatment groups is randomised

Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study. If there is no indication of randomisation, the study should be rejected. If the description of randomisation is poor, or the process used is not truly random (for example, allocation by date or alternating between one group and another) or can otherwise be seen as flawed, the study should be given a lower quality rating.

1.3 An adequate concealment method is used

Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%. Centralised allocation, computerised allocation systems or the use of coded identical containers would all be regarded as adequate methods of concealment and may be taken as indicators of a well-conducted study. If the method of concealment used is regarded as poor, or relatively easy to subvert, the study must be given a lower quality rating, and can be rejected if the concealment method is seen as inadequate.

1.4 Subjects and investigators are kept 'blind' about treatment allocation

Blinding can be carried out up to three levels. In single-blind studies, patients are unaware of which treatment they are receiving; in double-blind studies, the doctor and the patient are unaware of which treatment the patient is receiving; in triple-blind studies, patients, healthcare providers and those conducting the analysis are unaware of which patients receive which treatment. The higher the level of blinding, the lower the risk of bias in the study.

1.5 The treatment and control groups are similar at the start of the trial

Patients selected for inclusion in a trial should be as similar as possible, in order to eliminate any possible bias. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin or comorbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

1.6 The only difference between groups is the treatment under investigation

If some patients receive additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. If groups are not treated equally, the study should be rejected unless no other evidence is available. If the study is used as evidence, it should be treated with caution and given a low quality rating.

1.7 All relevant outcomes are measured in a standard, valid and reliable way

If some significant clinical outcomes have been ignored, or not adequately taken into account, the study should be downgraded. It should also be downgraded if the measures used are regarded as being doubtful in any way or applied inconsistently.

1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?

The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop-out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients drop out, as well as how many. It should be noted that the drop-out rate may be expected to be higher in studies conducted over a long period of time. A higher drop-out rate will normally lead to downgrading, rather than rejection, of a study.

1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis)

In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contraindications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated, irrespective of the treatment they actually received. (This is known as intention-to-treat analysis.) If it is clear that analysis is not on an intention-to-treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

1.10 Where the study is carried out at more than one site, results are comparable for all sites

In multi-site studies, confidence in the results should be increased if it can be shown that similar results have been obtained at the different participating centres.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on the responses in Section 1 and using the following coding system:

++	All or most of the criteria have been fulfilled. Where they have not been fulfilled, the conclusions of the study or review are thought **very unlikely** to alter.
+	Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.
–	Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

Quality Checklist for a Cohort Study*		
Study ID:		Relevant questions:
Guideline topic:		
Checklist completed by:		
SECTION 1: INTERNAL VALIDITY		
In a well conducted cohort study:		**In this study the criterion is:** **(*Circle one option for each question)***
1.1	The study addresses an appropriate and	Well covered Not addressed

	clearly focused question.	Adequately addressed Poorly addressed	Not reported Not applicable
SELECTION OF SUBJECTS			
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?		
1.6	Comparison is made between full participants and those lost to follow-up, by exposure status.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
ASSESSMENT			
1.7	The outcomes are clearly defined.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	The assessment of outcome is made blind to exposure status.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.10	The measure of assessment of exposure is reliable.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

1.12	Exposure level or prognostic factor is assessed more than once.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
CONFOUNDING			
1.13	The main potential confounders are identified and taken into account in the design and analysis.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
STATISTICAL ANALYSIS			
1.14	Have confidence intervals been provided?		
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise the risk of bias or confounding, and to establish a causal relationship between exposure and effect? *Code* ++, + *or* –		

*A cohort study can be defined as a retrospective or prospective follow-up study. Groups of individuals are defined on the basis of the presence or absence of exposure to a suspected risk factor or intervention. This checklist is not appropriate for assessing uncontrolled studies (for example, a case series where there is no comparison [control] group of patients).

Notes on the use of the methodology checklist: cohort studies

The studies covered by this checklist are designed to answer questions of the type 'What are the effects of this exposure?' It relates to studies that compare a group of people with a particular exposure with another group who either have not had the exposure or have a different level of exposure. Cohort studies may be prospective (where the exposure is defined and subjects selected before outcomes occur) or retrospective (where exposure is assessed after the outcome is known, usually by the examination of medical records). Retrospective studies are generally regarded as a weaker design, and should not receive a 2++ rating.

Section 1 identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review —that is, making sure that it has been carried out carefully, and that the outcomes are likely to be attributable to the intervention being investigated. Each question covers an aspect of methodology that has been shown to make a significant difference to the conclusions of a study.

Because of the potential complexity and subtleties of the design of this type of study, there are comparatively few criteria that automatically rule out use of a study as evidence. It is more a matter of increasing confidence in the likelihood of a causal relationship existing between exposure and outcome by identifying how many aspects of good study design are present and how well they have been tackled. A study that fails to address or report on more than one or two of the questions considered below should almost certainly be rejected.

For each question in this section, one of the following should be used to indicate how well it has been addressed in the review:

- well covered
- adequately addressed
- poorly addressed
- not addressed (that is, not mentioned or indicates that this aspect of study design was ignored)
- not reported (that is, mentioned but insufficient detail to allow assessment to be made)
- not applicable.

1.1 The study addresses an appropriate and clearly focused question

Unless a clear and well-defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question to be answered on the basis of its conclusions.

1.2 The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation

Study participants may be selected from the target population (all individuals to which the results of the study could be applied), the source population (a defined subset of the target population from which participants are selected) or from a pool of eligible subjects (a clearly defined and counted group selected from the source population). It is important that the two groups selected for comparison are as similar as possible in all characteristics except for their exposure status or the presence of specific prognostic factors or prognostic markers relevant to the study in question. If the study does not include clear definitions of the source populations and eligibility criteria for participants, it should be rejected.

1.3 The study indicates how many of the people asked to take part did so in each of the groups being studied

This question relates to what is known as the participation rate, defined as the number of study participants divided by the number of eligible subjects. This should be calculated separately for each branch of the study. A large difference in participation rate between the two arms of the study indicates that a significant degree of selection bias may be present, and the study results should be treated with considerable caution.

1.4 The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis

If some of the eligible subjects, particularly those in the unexposed group, already have the outcome at the start of the trial, the final result will be biased. A well-conducted study will attempt to estimate the likelihood of this occurring and take it into account in the analysis through the use of sensitivity studies or other methods.

1.5 What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?

The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop-out rate is regarded as acceptable, but in observational studies conducted over a lengthy period of time a higher drop-out rate is to be expected. A decision on whether to downgrade or reject a study because of a high drop-out rate is a

matter of judgement based on the reasons why people drop out and whether drop-out rates are comparable in the exposed and unexposed groups. Reporting of efforts to follow up participants that drop out may be regarded as an indicator of a well-conducted study.

1.6 Comparison is made between full participants and those lost to follow-up by exposure status

For valid study results, it is essential that the study participants are truly representative of the source population. It is always possible that participants who drop out of the study will differ in some significant way from those who remain part of the study throughout. A well-conducted study will attempt to identify any such differences between full and partial participants in both the exposed and unexposed groups. Any indication that differences exist should lead to the study results being treated with caution.

1.7 The outcomes are clearly defined

Once enrolled in the study, participants should be followed until specified end points or outcomes are reached. In a study of the effect of exercise on the death rates from heart disease in middle-aged men, for example, participants might be followed up until death, reaching a predefined age or until completion of the study. If outcomes and the criteria used for measuring them are not clearly defined, the study should be rejected.

1.8 The assessment of outcome is made blind to exposure status

If the assessor is blinded to which participants received the exposure, and which did not, the prospects of unbiased results are significantly increased. Studies in which this is done should be rated more highly than those where it is not done or not done adequately.

1.9 Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome

Blinding is not possible in many cohort studies. In order to assess the extent of any bias that may be present, it may be helpful to compare process measures used on the participant groups — for example, frequency of observations, who carried out the observations and the degree of detail and completeness of observations. If these process measures are comparable between the groups, the results may be regarded with more confidence.

1.10 The measure of assessment of exposure is reliable

A well-conducted study should indicate how the degree of exposure or presence of prognostic factors or markers was assessed. Whatever measures are used must be sufficient to establish clearly that participants have or have not received the exposure under investigation and the extent of such exposure, or that they do or do not possess a particular prognostic marker or factor. Clearly described, reliable measures should increase the confidence in the quality of the study.

1.11 Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable

The inclusion of evidence from other sources or previous studies that demonstrate the validity and reliability of the assessment methods used should further increase confidence in study quality.

1.12 Exposure level or prognostic factor is assessed more than once

Confidence in data quality should be increased if exposure level or the presence of prognostic factors is measured more than once. Independent assessment by more than one investigator is preferable.

1.13 The main potential confounders are identified and taken into account in the design and analysis

Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The report of the study should indicate which potential confounders have been considered and how they have been assessed or allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected, depending on how serious the risk of confounding is considered to be. A study that does not address the possibility of confounding should be rejected.

1.14 Have confidence intervals been provided?

Confidence limits are the preferred method for indicating the precision of statistical results and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with caution.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on the responses in Section 1 and using the following coding system:

++	All or most of the criteria have been fulfilled. Where they have not been fulfilled, the conclusions of the study or review are thought **very unlikely** to alter.
+	Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.
–	Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

Appendix 12: Search strategies for the identification of health economics evidence

The search strategies should be referred to in conjunction with information set out in Section 3.2.16.

For standard mainstream bibliographic databases (CINAHL, EMBASE, MEDLINE and PsycINFO) search terms on alcohol dependence and harmful alcohol use were combined with a search filter for health economic studies. For searches generated in topic-specific databases (HTA, NHS EED) search terms on alcohol dependence and harmful alcohol use were used without a filter. The search strategies were initially developed for Medline before being translated for use in other databases/interfaces.

A condensed version of the strategies constructed for use with the main databases searched follows:

1. Guideline topic search strategy

a. MEDLINE, EMBASE, PsycINFO - Ovid SP interface

1. exp alcohol abuse/ or (alcohol-related disorders or alcohol-induced disorders or sobriety).sh.
2. (alcoholi$ or (alcohol$ and (abstinence or detoxification or intoxicat$ or rehabilit$ or withdraw$))).hw.
3. alcoholi$.ti,ab.
4. (drinker$1 or (drink$ adj2 use$1) or ((alcohol$ or drink$) adj5 (abstinen$ or abstain$ or abus$ or addict$ or attenuat$ or binge$ or crav$ or dependen$ or detox$ or disease$ or disorder$ or excessiv$ or harm$ or hazard$ or heavy or high risk or intoxicat$ or misus$ or overdos$ or (over adj dos$) or problem$ or rehab$ or reliance or reliant or relaps$ or withdraw$))).ti,ab.
5. (control$ adj2 drink$).tw.
6. sobriet$.ti,ab,hw.
7. or/1-6

b. CINAHL - Ebsco interface

S10 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9
S9 TI sobriet* or AB sobriet*
S8 (TI control* N2 drink*) or (AB control* N2 drink*)
S7 (TI drink* N5 abstinen* or AB drink* N5 abstinen*) or (TI drink* N5 abstain* or AB drink* N5 abstain*) or (TI drink* N5 abus* or AB drink* N5 abus*) or (TI drink* N5 addict* or AB drink* N5 addict*) or (TI drink* N5 attenuat* or AB drink* N5 attenuat*) or (TI drink* N5 binge* or AB drink* N5 binge*) or (TI drink* N5 crav* or AB drink* N5 crav*) or (TI drink* N5 dependen* or AB drink* N5 dependen*) or (TI drink* N5 detox* or AB drink* N5 detox*) or (TI drink* N5 disease* or AB drink* N5 disease*) or (TI drink* N5 disorder* or AB drink* N5 disorder*) or (TI

drink* N5 excessiv* or AB drink* N5 excessiv*) or (TI drink* N5 harm* or AB drink* N5 harm*) or (TI drink* N5 hazard* or AB drink* N5 hazard*) or (TI drink* N5 heavy or AB drink* N5 heavy) or (TI drink* N5 high risk or AB drink* N5 high risk) or (TI drink* N5 intoxicat* or AB drink* N5 intoxicat*) or (TI drink* N5 misus* or AB drink* N5 misus*) or (TI drink* N5 overdos* or AB drink* N5 overdos*) or (TI drink* N5 over dos* or AB drink* N5 over dos*) or (TI drink* N5 problem* or AB drink* N5 problem*) or (TI drink* N5 rehab* or AB drink* N5 rehab*) or (TI drink* N5 reliance or AB drink* N5 reliance) or (TI drink* N5 reliant or AB drink* N5 reliant) or (TI drink* N5 relaps* or AB drink* N5 relaps*) or (TI drink* N5 withdraw* or AB drink* N5 withdraw*)

S6 (TI alcohol* N5 abstinen* or AB alcohol* N5 abstinen*) or (TI alcohol* N5 abstain* or AB alcohol* N5 abstain*) or (TI alcohol* N5 abus* or AB alcohol* N5 abus*) or (TI alcohol* N5 addict* or AB alcohol* N5 addict*) or (TI alcohol* N5 attenuat* or AB alcohol* N5 attenuat*) or (TI alcohol* N5 binge* or AB alcohol* N5 binge*) or (TI alcohol* N5 crav* or AB alcohol* N5 crav*) or (TI alcohol* N5 dependen* or AB alcohol* N5 dependen*) or (TI alcohol* N5 detox* or AB alcohol* N5 detox*) or (TI alcohol* N5 disease* or AB alcohol* N5 disease*) or (TI alcohol* N5 disorder* or AB alcohol* N5 disorder*) or (TI alcohol* N5 excessiv* or AB alcohol* N5 excessiv*) or (TI alcohol* N5 harm* or AB alcohol* N5 harm*) or (TI alcohol* N5 hazard* or AB alcohol* N5 hazard*) or (TI alcohol* N5 heavy or AB alcohol* N5 heavy) or (TI alcohol* N5 high risk or AB alcohol* N5 high risk) or (TI alcohol* N5 intoxicat* or AB alcohol* N5 intoxicat*) or (TI alcohol* N5 misus* or AB alcohol* N5 misus*) or (TI alcohol* N5 overdos* or AB alcohol* N5 overdos*) or (TI alcohol* N5 over dos* or AB alcohol* N5 over dos*) or (TI alcohol* N5 problem* or AB alcohol* N5 problem*) or (TI alcohol* N5 rehab* or AB alcohol* N5 rehab*) or (TI alcohol* N5 reliance or AB alcohol* N5 reliance) or (TI alcohol* N5 reliant or AB alcohol* N5 reliant) or (TI alcohol* N5 relaps* or AB alcohol* N5 relaps*) or (TI alcohol* N5 withdraw* or AB alcohol* N5 withdraw*)

S5 (TI drink* N2 use*) or (AB drink* N2 use*)

S4 TI drinker* or AB drinker*

S3 MW alcoholi*

S2 MW alcohol* and (abstinence or detoxification or intoxicat* or rehabilit* or withdraw*)

S1 (MH "Alcohol Abuse") or (MH "Alcoholic Intoxication") or (MH "Alcoholism") or (MH "Alcohol-Related Disorders") or (MH "Alcohol Abuse Control (Saba CCC)") or (MH "Alcohol Abuse (Saba CCC)")

c. Health Technology Assessment Database, NHS Economic Evaluation Database - Wiley Interscience interface

#1 MeSH descriptor Alcohol-Related Disorders, this term only

#2 MeSH descriptor Alcohol-Induced Disorders, this term only

#3 MeSH descriptor Alcoholic Intoxication, this term only

#4 MeSH descriptor Alcoholism, this term only

#5 (alcoholi*):ti or (alcoholi*):ab

#6 (abstinence or detoxification or intoxicat* or rehabilit* or withdraw*):kw and

(alcohol*):kw
#7 MeSH descriptor Substance-Related Disorders, this term only
#8 (drinker* or (drink* NEAR/2 use*) or ((alcohol* or drink*) NEAR/5 (abstinen* or abstain* or abus* or addict* or attenuat* or binge* or crav* or dependen* or detox* or disease* or disorder* or excessiv* or harm* or hazard* or heavy or high risk or intoxicat* or misus* or overdos* or over dose or over dosing or over doses or problem* or rehab* or reliance or reliant or relaps* or withdraw*))):ti or (drinker* or (drink* NEAR/2 use*) or ((alcohol* or drink*) NEAR/5 (abstinen* or abstain* or abus* or addict* or attenuat* or binge* or crav* or dependen* or detox* or disease* or disorder* or excessiv* or harm* or hazard* or heavy or high risk or intoxicat* or misus* or overdos* or over dose or over dosing or over doses or problem* or rehab* or reliance or reliant or relaps* or withdraw*))):ab
#9 (control* NEAR/2 drink*):ti or (control* NEAR/2 drink*):ab
#10 (sobriet*):ti or (sobriet*):ab
#11 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)

2 Health economics and quality-of-life search filter – this is an adaptation of a filter designed by the NHS Centre for Reviews and Dissemination at the University of York.

a. MEDLINE, EMBASE, PsycINFO - Ovid SP interface

1 (health care rationing or health priorities or medical savings accounts or resource allocation).sh,id. or "deductibles and coinsurance"/
2 (budget$ or cost$ or econom$ or expenditure$ or fee$1 or financ$ or health resource or money or pharmacoeconomic$ or socioeconomic).hw,id.
3 (budget$ or cost$ or econom$ or expenditure$ or financ$ or fiscal or funding or pharmacoeconomic$ or socioeconomic$ or price or prices or pricing or (value adj3 money) or (burden adj3 (disease$ or illness$))).tw.
4 exp "quality of life"/ or "value of life"/ or (quality adjusted life year$ or well being or wellbeing).sh,id.
5 exp models, economic/ or (models, statistical or statistical model or (economics and models)).sh,id.
6 health status indicators.sh,id.
7 (daly or qol or hql or hqol or hrqol or hr ql or hrql or (quality adj2 life) or (adjusted adj2 life) or qaly$ or (health adj2 stat$) or well being or wellbeing or qald$ or qale$ or qtime$ or eq5d or eq 5d or qwb or ((quality or value$) adj3 (life or survival or well$)) or hui$1 or (utilit$ adj1 (health or score$ or weigh$)) or (life adj2 year$) or health year equivalent$ or ((disability or quality) adj adjusted) or utility value$ or (weight$ adj3 preference$) or euroqol or euro qol or visual analog$ or standard gamble or time trade or qtwist or q twist or (valu$ adj2 quality)).tw.
8 decision tree/ or decision trees/
9 (decision analy$ or monte carlo or markov or simulation model$ or rosser or disutili$ or willingness to pay or tto or hye or hyes or (resource adj (allocat$ or use$ or utilit$))).tw.
10 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw,tm,it.
11 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six

		or short form six).tw,tm,it.
	12	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw,tm,it.
	13	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw,tm,it.
	14	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw,tm,it.
	15	ec.fs. *[ANDed with subject heading searches for the main population/topic]*
	16	or/1-15
	17	animal$/ not human$.mp.
	18	animal$/ not human$/
	19	(animal not human).po.
	20	16 not (or/17-19)
		b. CINAHL — Ebsco interface
	S19	S17 not S18
	S18	(MH "Animals") not (MH "Human")
	S17	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16
	S16	ti ((sf20 or “sf 20” or “short form 20” or “shortform 20” or “sf twenty” or sftwenty or “shortform twenty” or “short form twenty”)) or ab ((sf20 or “sf 20” or “short form 20” or “shortform 20” or “sf twenty” or sftwenty or “shortform twenty” or “short form twenty”))
	S15	ti ((sf16 or “sf 16” or “short form 16” or “shortform 16” or “sf sixteen” or sfsixteen or “shortform sixteen” or “short form sixteen”)) or ab ((sf16 or “sf 16” or “short form 16” or “shortform 16” or “sf sixteen” or sfsixteen or “shortform sixteen” or “short form sixteen”))
	S14	ti ((sf12 or “sf 12” or “short form 12” or “shortform 12” or “sf twelve” or sftwelve or “shortform twelve” or “short form twelve”)) or ab ((sf12 or “sf 12” or “short form 12” or “shortform 12” or “sf twelve” or sftwelve or “shortform twelve” or “short form twelve”))
	S13	ti ((sf6 or “sf 6” or “short form 6” or “shortform 6” or “sf six” or sfsix or “shortform six” or “short form six”)) or ab ((sf6 or “sf 6” or “short form 6” or “shortform 6” or “sf six” or sfsix or “shortform six” or “short form six”))
	S12	ti ((sf36 or “sf 36” or “short form 36” or “shortform 36” or “sf thirtysix” or “sf thirty six” or “shortform thirtysix” or “shortform thirty six “ or “short form thirtysix” or “short form thirty six”)) or ab ((sf36 or “sf 36” or “short form 36” or “shortform 36” or “sf thirtysix” or “sf thirty six” or “shortform thirtysix” or “shortform thirty six “ or “short form thirtysix” or “short form thirty six”))
	S11	ti ((“decision analys*” or “monte carlo” or markov or “simulation model*” or rosser or disutili* or “willingness to pay” or tto or hye or hyes or “resource allocation” or “resource use” or “resource ulitit*”)) or ab ((“decision analys*” or “monte carlo” or markov or “simulation model*” or rosser or disutili* or “willingness to pay” or tto or hye or hyes or “resource allocation” or “resource use” or “resource ulitit*”))
	S10	(mh "decision trees")
	S9	TI (daly or qol or hql or hqol or hrqol or “hr ql” or hrql or qaly* or “well

		being" or wellbeing or qald* or qale* or qtime* or eq5d or "eq 5d" or qwb or hui or "health year equivalent*" or "utility value*" or euroqol or "euro qol" or "visual analog*" or "standard gamble" or "time trade" or qtwist or "q twist" or "disability adjusted" or "quality adjusted") or AB (daly or qol or hql or hqol or hrqol or "hr ql" or hrql or qaly* or "well being" or wellbeing or qald* or qale* or qtime* or eq5d or "eq 5d" or qwb or hui or "health year equivalent*" or "utility value*" or euroqol or "euro qol" or "visual analog*" or "standard gamble" or "time trade" or qtwist or "q twist" or "disability adjusted" or "quality adjusted") or (TI quality N2 life or AB quality N2 life) or (TI adjusted N2 life or AB adjusted N2 life) or (TI health N2 stat* or AB health N2 stat*) or (TI quality N3 life or AB quality N3 life) or (TI quality N3 survival or AB quality N3 survival) or (TI quality N3 well* or AB quality N3 well*) or (TI value N3 life or AB value N3 life) or (TI value N3 survival or AB value N3 survival) or (TI value N3 well* or AB value N3 well*) or (TI utilit* N1 health or AB utilit* N1 health) or (TI utilit* N1 score* or AB utilit* N1 score*) or (TI utilit* N1 weigh* or AB utilit* N1 weigh*) or (TI life N2 year* or AB life N2 year*) or (TI weight* N3 preference* or AB weight* N3 preference*) or (TI valu* N2 quality or AB valu* N2 quality)
	S8	(mh "health status indicators") or (MH "Models, Statistical")
	S7	(mh "psychological well-being") or (MH "Psychological Well-Being (Iowa NOC) (Non-Cinahl)") or (MH "Well-Being (Iowa NOC)")
	S6	(mh "quality of life+") or (MH "Economic Value of Life") or (MH "Quality-Adjusted Life Years")
	S5	TI (budget* or cost* or econom* or expenditure* or financ* or fiscal or funding or pharmacoeconomic* or socioeconomic* or price or prices or pricing) or AB (budget* or cost* or econom* or expenditure* or financ* or fiscal or funding or pharmacoeconomic* or socioeconomic* or price or prices or pricing) or ((TI value N3 money or AB value N3 money) or (TI burden N3 disease* or AB burden N3 disease*) or (TI burden N3 illness* or AB burden N3 illness*))
	S4	mw (budget* or cost* or econom* or expenditure* or fee* or financ* or health resource or money or pharmacoeconomic* or socioeconomic)
	S3	(mh "economic value of life")
	S2	(mh "resource allocation") or (mh "health resource allocation")
	S1	(mh "medical savings accounts")

Details of searches undertaken in EconLit are available on CD/on request.

Appendix 13: Quality checklists for economic studies

This checklist is designed to determine whether an economic evaluation provides evidence that is useful to inform the decision-making of the Guideline Development Group (GDG). It is not intended to judge the quality of the study per se or the quality of reporting.

Section 1: Applicability (relevance to specific guideline review question(s) and the NICE reference case) This checklist should be used first to filter out irrelevant studies.	**Yes/ Partly/ No /Unclear /NA**	**Comments**
1. Is the patient population appropriate for the guideline?		
2. Are the interventions appropriate for the guideline?		
3. Is the healthcare system in which the study was conducted sufficiently similar to the current UK NHS context?		
4. Are costs measured from the NHS and PSS perspective?		
5. Are all health effects on individuals included?		
6. Are both costs and health effects discounted at an annual rate of 3.5%?		
7. Is the value of health effects expressed in terms of QALYs?		
8. Are changes in health related quality of life (HRQL) reported directly from patients and/or carers?		
9. Is the value of changes in HRQL (that is utilities) obtained from a representative sample of the public?		
10. **Overall judgement**: Directly applicable/Partially applicable/Not applicable		
Other comments:		

Section 2: Study limitations (the level of methodological quality) This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline.	**Yes/ Partly /No/ Unclear/NA**	**Comments**

1. Does the model structure adequately reflect the nature of the health condition under evaluation?		
2. Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?		
3. Are all important and relevant health outcomes included?		
4. Are the estimates of baseline health outcomes from the best available source?		
5. Are the estimates of relative treatment effects from the best available source?		
6. Are all important and relevant costs included?		
7. Are the estimates of resource use from the best available source?		
8. Are the unit costs of resources from the best available source?		
9. Is an appropriate incremental analysis presented or can it be calculated from the data?		
10. Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?		
11. Is there no potential conflict of interest?		
12. **Overall assessment**: Minor limitations/Potentially serious limitations/Very serious limitations		
Other comments:		

1

1.2 Partial economic evaluations

Author: **Date:**

Title:

	Study design	Yes	No	NA
1	The research question is stated	❑	❑	
2	The viewpoint(s) of the analysis is clearly stated and justified	❑	❑	
	Data collection			
1	Details of the subjects from whom valuations were obtained are given	❑	❑	
2	Indirect costs (if included) are reported separately	❑	❑	❑
3	Quantities of resources are reported separately from their unit costs	❑	❑	
4	Methods for the estimation of quantities and unit costs are described	❑	❑	
5	Currency and price data are recorded	❑	❑	
6	Details of currency of price adjustments for inflation or currency conversion are given	❑	❑	❑
7	Details of any model used are given	❑	❑	❑
8	The choice of model used and the key parameters on which it is based are justified	❑	❑	❑
	Analysis and interpretation of results			
1	Time horizon of costs is stated	❑	❑	
2	The discount rate(s) is stated	❑	❑	❑
3	Details of statistical tests and confidence intervals are given for stochastic data	❑	❑	❑
4	The choice of variables for sensitivity analysis is given	❑	❑	
5	The ranges over which the variables are varied are stated	❑	❑	
6	Appropriate sensitivity analysis is performed	❑	❑	
7	The answer to the study question is given	❑	❑	
8	Conclusions follow from the data reported	❑	❑	
9	Conclusions are accompanied by the appropriate caveats	❑	❑	

Appendix 14: Data extraction form for economic studies

Reviewer: **Date of Review:**

Authors:

Publication Date:

Title:

Country:

Language:

Economic study design:

- ❑ CEA
- ❑ CBA
- ❑ CUA
- ❑ CMA
- ❑ CCA
- ❑ CA

Modelling:

- ❑ No
- ❑ Yes

Source of data for effect size measure(s):

	❑ Meta-analysis
❑ RCT	❑ RCT
❑ Quasi experimental study	❑ Quasi experimental study
❑ Cohort study	❑ Cohort study
❑ Mirror image (before-after) study	❑ Mirror image (before-after) study
	❑ Expert opinion

Comments _____

Primary outcome measure(s) (please list):

_____

Interventions compared (please describe):

Treatment: _____

Comparator: _____

Setting (please describe):

_____

_____

Patient population characteristics (please describe):

_____

_____

_____

Perspective of analysis:

❑ Societal ❑ Other: _____

❑ Patient and family

❑ Health care system

❑ Health care provider

❑ Third party payer

Time frame of analysis: _____

Cost data:

❑ Primary ❑ Secondary

If secondary please specify: _____

Costs included:

Direct medical	Direct non-medical	Lost productivity
❑ direct treatment	❑ social care	❑ income forgone due to illness
❑ inpatient	❑ social benefits	❑ income forgone due to death
❑ outpatient	❑ travel costs	❑ income forgone by caregiver
❑ day care	❑ caregiver out-of-pocket	
❑ community health care	❑ criminal justice	
❑ medication	❑ training of staff	

Or

❑ staff

❑ medication

❑ consumables

❑ overhead

❑ capital equipment

❑ real estate Others: _____

Currency: _____ **Year of costing:** _____

Was discounting used?

❑ Yes, for benefits and costs ❑ Yes, but only for costs ❑ No

Discount rate used for costs:

Discount rate used for benefits: _____

Result(s):

Comments, limitations of the study:

Quality checklist score (Yes/NA/All): ……/……/……

Appendix 15. Network meta-analysis for the economic model

This section outline the network meta-analysis undertaken for the economic model assessing the cost effectiveness of pharmacological interventions for relapse prevention in people in recovery from alcohol dependence

Clinical data considered in the network meta-analysis

Clinical data for the network meta-analysis were derived from trials included in the guideline systematic literature review on pharmacological interventions for relapse prevention in people in recovery from alcohol dependence. This review included 33 RCTs that reported relapse data for one or more of the interventions assessed in the economic analysis. The evidence network constructed based on the available data is shown in Figure 1. Inspection of the network and the available evidence indicated that 32 studies contributed to provision of direct or indirect evidence on the relative effect between the 3 interventions assessed in the economic model, and thus should be considered in network meta-analysis. The time horizon of these studies ranged from 3 to 12 months. Table 1 provides the relapse data included in the network meta-analysis the studies, as well as the time horizons of the studies considered.

Figure 11. Evidence network for data on relapse to alcohol dependence

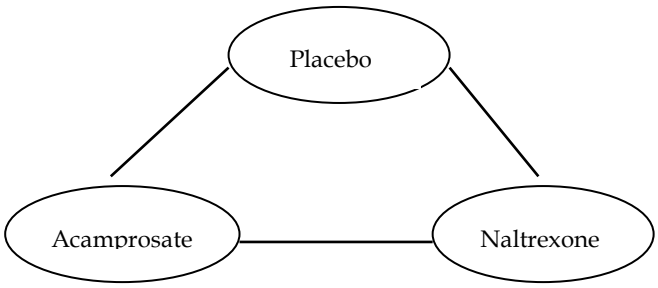


Table 109. Summary of the data reported in the RCTs included in the guideline systematic review on rates of relapse to alcohol dependence usedcin the network meta-analysis

Study	Timepoint (Months)	Comparators	Number of people relapsing (r)	Number of people in each arm (n)
1. Anton, 1999	3	1) Placebo 2) Naltrexone	38 26	63 68
2. Anton, 2005	3	1) Placebo 2) Naltrexone	47 33	80 80
3. Anton, 2006	12	1) Placebo 2) Naltrexone 3) Acamprosate	126 122 117	156 155 151
4. Balldin, 2003	3	1) Placebo 2) Naltrexone	58 53	62 56
5. Besson, 1998	12	1) Placebo 3) Acamprosate	47 41	55 55
6. Chick, 2000a	3	1) Placebo 2) Naltrexone	61 64	85 90

7. Chick, 2000b	6	1) Placebo 3) Acamprosate	242 245	292 289
8. Gastpar, 2002	3	1) Placebo 2) Naltrexone	36 34	87 84
9. Geerlings, 1997	6	1) Placebo 3) Acamprosate	116 96	134 128
10. Guardia, 2002	3	1) Placebo 2) Naltrexone	19 8	99 93
11. Heinala, 2001	3	1) Placebo 2) Naltrexone	54 52	58 63
12. Huang, 2005	3	1) Placebo 2) Naltrexone	4 3	20 20
13. Kiefer, 2003	6	1) Placebo 2) Naltrexone 3) Acamprosate	32 21 22	40 40 40
14. Killeen, 2004	3	1) Placebo 2) Naltrexone	12 21	36 51
15. Krystal, 2001	3	1) Placebo 2) Naltrexone	83 143	187 378
16. Latt, 2002	3	1) Placebo 2) Naltrexone	27 19	51 56
17. Lee, 2001	3	1) Placebo 2) Naltrexone	8 8	15 24
18. Monti, 2001	3	1) Placebo 2) Naltrexone	21 18	64 64
19. Morley, 2006	3	1) Placebo 2) Naltrexone 3) Acamprosate	43 39 40	61 53 55
20. Morris, 2001	3	1) Placebo 2) Naltrexone	26 19	33 38
21. O'Malley, 2008	3	1) Placebo 2) Naltrexone	28 22	34 34
22. Oslin, 1997	3	1) Placebo 2) Naltrexone	8 3	23 21
23. Oslin, 2008	6	1) Placebo 2) Naltrexone	76 73	120 120
24. Paille, 1995	12	1) Placebo 3) Acamprosate	144 113	177 173
25. Pelc, 1992	6	1) Placebo 3) Acamprosate	43 35	47 55
26. Pelc, 1997	3	1) Placebo 3) Acamprosate	46 31	62 63
27. Poldrugo, 1997	6	1) Placebo 3) Acamprosate	79 58	124 122
28. Sass, 1996	6	1) Placebo 3) Acamprosate	105 73	138 137
29. Tempesta, 2000	6	1) Placebo 3) Acamprosate	61 49	166 164
30. Volpicelli, 1992	3	1) Placebo 2) Naltrexone	19 8	35 35
31. Volpicelli, 1997	3	1) Placebo 2) Naltrexone	26 17	49 48
32. Whitworth, 1996	12	1) Placebo 3) Acamprosate	139 129	224 224

1

Network meta-analysis – full random effects model

A full random effects model (model 1) was constructed to estimate the relative effect between the k=3 interventions assessed, using data from the 32 RCTs summarised in table 1. The data for each trial j comprised a binomial likelihood:

$$r_{jk} \sim \text{Bin}\ (p_{jk},\ n_{jk})$$

where p_{jk} is the probability of relapse in trial j under treatment k, r_{jk} is the number of people experiencing relapse in trial j under treatment k, and n_{jk} is the total number of people at risk of relapse in trial j under treatment k.

The duration of the trials considered in the analysis varied from 3 to 12 months. The model assumed constant hazards $\exp(\theta_{jk})$ acting over a period T_j in months. Thus, the probability of relapse by the end of the period T_j for treatment k in trial j was:

$$p_{jk}(T_j) = 1 - \exp\ (-\exp(\theta_{jk})\ T_j)$$

Treatment effects were modelled on the log-hazard rate scale and were assumed to be additive to the baseline treatment b in trial j:

$$\theta_{jk} = \mu_{jb} \qquad \text{for } k = b;$$
$$\theta_{jk} = \mu_{jb} + \delta_{jkb} \qquad \text{for } k \neq b$$

where μ_{jb} is the log hazard of relapse for 'baseline' treatment b in trial j and δ_{jkb} is the trial-specific log-hazard ratio of treatment k relative to treatment b.

The full random effects model took into account the correlation structure induced by 3 multi-arm trials included in the 32 RCTs; this type of model structure relies on the realisation of the bivariate normal distribution as a univariate marginal distribution and a univariate conditional distribution (Higgins & Whitehead, 1996):

$$\text{If} \quad \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} \sim N\left[\begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix}, \begin{pmatrix} \sigma^2 & \sigma^2/2 \\ \sigma^2/2 & \sigma^2 \end{pmatrix}\right]$$

$$\text{then} \quad x_1 \sim N\ (\mu_1\ ,\ \sigma^2), \quad \text{and} \quad x_2 \mid x_1 \sim N\ (\mu_2 + \frac{1}{2}(x_1 - \mu_1), \frac{3}{4}\sigma^2)$$

The trial-specific log-hazard ratios for every pair of interventions were assumed to come from a normal random effects distribution:

$$\delta_{jkb} \sim \textit{Normal}\ (d_{kb},\ \sigma^2)$$

The mean of this distribution (d_{kb}) is the true mean effect size between k and b and σ^2 *is* the variance of the normal distribution which was assumed to be common in all pairs of treatments.

Vague priors were assigned to trial baselines, mean treatment effects and common variance:

$$\mu_{jb,}\, d_{kb} \sim Normal\ (0, 100^2); \quad \sigma \sim Uniform\ (0,2)$$

A separate random effects model (model 2) was constructed to estimate the baseline placebo effect, using relapse data from the 32 trials with a placebo arm included in the guideline systematic review. The placebo effect (φ_j) was again modelled on a log hazard scale and was assumed to come from a normal random effects distribution:

$$\varphi_j \sim Normal\ (B, \omega^2)$$

$$B \sim Normal\ (0, 100^2); \omega \sim Uniform\ (0,2)$$

$$p_j(T_j) = 1 - \exp\ (-\exp(\varphi_j)\ T_j)$$

Subsequently, the absolute log hazard θ_{jk} of each drug k was estimated based on the treatment effect relative to placebo (estimated in model 1) added to a random value of the absolute log hazard of placebo (estimated in model 2). The output of the model that was used in the economic analysis was the probability of relapse for each intervention by the end of 12 months.

Analysis was undertaken following Bayesian statistics principles and conducted using Markov chain Monte Carlo simulation techniques implemented in Winbugs 1.4 (Lunn *et al.*, 2000; Spiegelhalter *et al.*, 2001). The first 60,000 iterations were discarded, and 300,000 further iterations were run; because of high autocorrelation observed in some model parameters, the model was thinned so that every 30th simulation was retained. Consequently, 10,000 posterior simulations were recorded.

The goodness of fit of the model to the data was measured by calculating the residual deviance defined as the difference between the deviance for the fitted model and the deviance for the saturated model, where the deviance measures the fit of the model to the data points using the likelihood function. Under the null hypothesis that the model provides an adequate fit to the data, it is expected that residual deviance would have a mean equal to the number of unconstrained data points (Cooper *et al.*, 2006). The residual deviance was calculated to be 44.86. This corresponds reasonably well with the number of unconstrained data points (67) of the model.

The Winbugs code used to estimate the 12-month probability of relapse is provided in Table 2. Table 3 provides summary statistics of a number of model parameters, including the log hazard ratios of the two drugs versus placebo and the between-trials variation. Results are reported as mean values with 95% credible intervals, which are analogous to confidence intervals in frequentist statistics.

Table 110. WinBUGs code used for network meta-anlysis to estimate 12-month probability of relapse

```
model{
sw[1] <- 0
for(i in 1:67){
r[i] ~ dbin(p[i],n[i])                                  #binomial likelihood
```

```
theta[i]<-mu[s[i]]+ delta[i]*(1-equals(t[i],b[i]))              #baseline and treatment effects
delta[i] ~ dnorm(md[i],taud[i])                                 #trial-specific log-hazard
distributions
taud[i] <- tau * (1 + equals(m[i],3) /3)                        #precisions of log-hazard
distributions
md[i] <- d[t[i]] - d[b[i]] + equals(m[i],3) * sw[i]                    #mean of random effect

p[i] <- (1-exp(-lam[i]*w[i]/360))  # pr of event (w=days; 360 days = 12 mths)
log(lam[i]) <- theta[i]                         # log rates for each arm

rhat[i] <- p[i] * n[i]                                  #predicted events

dev[i] <- -2 *r[i]*log(rhat[i]/r[i])                #deviance residuals for data i
}
resdev <-sum(dev[])                             #total deviance

for (i in 2:67) { sw[i] <- (delta[i-1] - d[t[i-1]] + d[b[i-1]] ) /2}     #adjustment for 3 arm trials

#priors
for(j in 1:32){ mu[j]~dnorm(0,.0001)}                       #vague priors for trial baselines
tau <- 1/(sd*sd)                                    #precision
sd~dunif(0,2)                                   #  vague prior for random effects standard
deviation

d[1]<-0
for (k in 2:3){d[k] ~ dnorm(0,.0001)#vague priors for basic parameters
log(hazr[k]) <-d[k]                             #hazard ratios
 }

#code for absolute effects on baseline (placebo, treatment 1)
for (i in 1:33) {
rb[i] ~ dbin(pb[i],nb[i])                   #binomial likelihood
pb[i] <- (1-exp(-lamb[i]*wb[i]/360))        # probability of event (w=days; 360 days = 12
mths)
log(lamb[i]) <- mub[sb[i]]                      # log rate
}

for (j in 1:33) {mub[j] ~ dnorm(mb,tab)}            # priors for outcome and trial-specific
events
mb ~ dnorm(0,.001)
tab <- 1/(sdb*sdb)
sdb ~ dunif(0,2)

#code for predicted effects at 360 days, on a probability scale. Baseline risks in mub[33] -
new trial
d.new[1] <-0
for(k in 2:3)
{d.new[k] ~ dnorm(d[k],tau)}
for (k in 1:3)
{theta360[k] <-mub[33] +d.new[k]
```

```
log(lam360[k]) <-theta360[k]
p360[k] <- (1-exp(-lam360[k]))
}

# prob that treatment k is best
  for (k in 1:3)  { rk[k]  <- rank(d[],k)
  best[k]  <- equals(rk[k],1)                    #Smallest is best (i.e. rank 1)
  for (h in 1:3) { prob[h,k] <- equals(rk[k],h) }}
}
#initial values 1
list(
d=c(NA,0,0),sd=1,mu=c(0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,
0,0),delta=c(0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,
0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0, 0,0,0,0,0,  0,0,0,0,0, 0,0), sdb=1,
mub=c(NA,0,0,0,0, 0,0,0,0,0,    0,0,0,0,0,    0,0,0,0,0,    0,0,0,0,0,    0,0,0,0,0,   0,0,  NA),
mb=1
)

#initial values 2
list(
d=c(NA,1,-1),sd=1.2,mu=c(0,0.5,0,2,0,0,  1,-1,-1,0,0,  -1,-1,-1,0,0,  1,1,1,0,-0.5,
0,1,-1,0,1,  0.5,2,1,0.3, 0.2, 0.1),delta=c(0.5,0.5,0.6,0.4,0.3,  1,-1,-1,-1,-1,  0,1,0.3,0.2,0,  -0.5,0,-1,-
1,-1,  1,1,1,-1,0.1,  0.1,1,-1,-0.1,0,  0,1,1.5,0,-1,  -1,0,1,1,1,  1,-0.1,0.5,0,1,  0,1,1,1,1,  -1,-1,-1,0,0,
1,1,1,0.5,0.5,  0,1,0,1,0, 0,1), sdb=0.7,mub=c(NA,0.5,0.7,-1,0.2,    0.05,0.4,1,1,  1, -1,0.3,1,1,
0.2,0.3,0.4,-1,-1,  0.2,0.3,0.4,1.1,0.5,  -0.2,0,-1,0,-1,  0,0.4,-0.2, NA),mb=0.5
)
```

Table 111. Summary statistics estimated from Network meta-analysis

Node	Mean	SD	MC error	25%	Median	75%	Start	Sample
p360[1]	0.8956	0.125	0.001383	0.5509	0.9433	1.0	60001	10000
p360[2]	0.8253	0.1656	0.001840	0.4095	0.8741	0.9997	60001	10000
p360[3]	0.8176	0.1691	0.001737	0.3894	0.8633	0.9996	60001	10000
sd	0.2043	0.05914	0.00084	0.0984	0.2011	0.3293	60001	10000
resdev	44.73	70.59	0.7011	-91.8	44.04	187.1	60001	10000

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